Innovation and new technologies to tackle infectious diseases of poverty
The traditional approach to tackling infectious diseases of poverty has been a disease-centred one but now, to benefit effectively from innovative products and use the tools needed to beat such diseases, the approach must be people-centred. In this chapter we explore how this might be achieved.
In a little over a century, knowledge in the fields of microbiology and parasitology, immunology and genetics, public health and medicine has increased exponentially. In combination with economic developments, this has resulted in many positive changes in human health: reductions in infant mortality, improved life expectancy, the near eradication of certain infectious diseases and the effective treatment of others. More recently, major advances in new fields and technologies, including genomics, proteomics, high-throughput screening, robotics, imaging and geographical information systems (GIS) have revolutionized drug discovery and the surveillance, prevention, treatment and control of new and emerging infectious diseases (1–3).

However, getting the right tools to those who need them most is not easy. Although government agencies and research institutes, private organizations, public–private partnerships (PPPs) and community-based organizations have all worked to reduce the burden of infectious diseases, the challenges persist. Life-saving innovations, including very simple yet effective interventions, still remain out of the reach of many. Many infectious diseases are still under-researched and poorly understood, and the innovations to address them are of limited commercial interest.

To reduce the burden of infectious disease and broker greater global equity, we need new levels of global commitment and new models of collaboration among stakeholders to bring about innovative solutions and to translate these solutions into effective programmes in settings where the needs are greatest. The challenge is more than the pursuit of technological marvels and “magic bullets”. It is about fostering a “culture of innovation”.

Innovation is about stimulating the search for novel discoveries; the development of technologies and tools for health interventions; understanding the specific social contexts in which interventions will be delivered; and strong engagement with communities to ensure maximum and sustainable implementation and uptake (4). Innovation is not just about doing things differently but also about doing things in a more sustainable, effective, safe and equitable manner.

In this chapter, we take a systems-based approach to innovation. We start by discussing how to create an environment of innovation in low and middle-income countries (LMICs), then examine how to foster innovative collaborations and product development for infectious diseases, the social innovations necessary for the uptake and delivery of health interventions, and how to build capacity in research and training in these countries.

**Understanding the health innovation system – navigating unchartered waters**

Health innovation systems acknowledge the interrelationship between education, research and development (R&D), manufacture, domestic and export markets, intellectual property and regulatory policies (5). These different components must be linked so that overall national and regional systems work efficiently and swiftly to respond to country and global health needs. Research plays a central role in an innovation system, from the inception of ideas to new ways of translation, policy design and regulation (6, 7).

For high-income countries, health innovation systems include actors from multiple sectors and disciplines. Conventionally, training and basic research are funded by the public sector through universities and government research institutions. Translational research and product development such as prototype productions or small-scale production are conducted by pharmaceutical or other companies or, depending on the national system, government institutions. In low-income countries, however, the health innovation system is often rudimentary and fragmented. The public sector provides most, if not all, funding and infrastructure for research. Although research is conducted in academic institutions, often there is little applicability to local health problems, due to the lack of capacity to conduct translational
research and limited manufacturing capacity. LMICs with some industry and manufacturing experience are usually limited to manufacturing low-technology products, or higher-technology products only under technology transfer agreements, rather than producing “home-grown” innovation for local health needs. The absence of private sector institutions engaging in health innovation also reflects limited expertise in product development, in regulatory and intellectual property management. This is partly due to the consistent drift of scientists to higher-income country research institutions, and partly due to lack of access to domestic and global markets. These factors represent major barriers to establishing and strengthening national innovation systems in LMICs. The various steps in the innovation value chain remain disconnected, impeding the progress of innovation in these countries.

Thus, unlike high-income countries, most LMICs have only a few areas of research and very limited development capacity. Resources in most other areas of innovations (e.g. intellectual property management and regulation, production and operation standards, and other social research) are also very limited. These scattered clusters of R&D-linked activities need to be connected in order to transform ideas and commitments towards innovative solutions (see Fig. 4.1).

Richard Mahoney and Carlos Morel argue that innovation disparity has created three kinds of “health failures” (4).

- **Science failures:** This refers to a lack of knowledge and tools to address health problems. For example, there are still no effective vaccines or drugs for infectious diseases such as dengue, tuberculosis (TB), malaria and trypanosomiasis.

---

**Fig. 4.1.** Disconnected value chain within the low and middle-income country health innovation system
Global initiatives to encourage innovation – turbo-charging

We are in the “era of partnerships” (4). Over the last two decades, product development partnerships involving the public and private sector have been formed to tackle diseases such as HIV, malaria, TB and, to a lesser extent, other infectious diseases. These partnerships include the International AIDS Vaccine Initiative (IAVI), International Partnership for Microbicides (IPM), Medicines for Malaria Venture (MMV), The Global Alliance for TB Drug Development (TB Alliance), Aeras Global TB Vaccine Foundation, Human Hookworm Vaccine Initiative (HHVI), Foundation for Innovative New Diagnostics (FIND), Drugs for Neglected Diseases initiative (DNDi) and OneWorld Health. The partnerships comprise multilateral agencies, foundations, donor countries and LMIC governments.

CASE STUDY 4.1

Can some infectious diseases be made history?

Many water-borne and vector-borne infectious diseases, such as guinea worm, schistosomiasis, lymphatic filariasis and onchocerciasis, could be controlled effectively by 2015, the target date for reaching the Millennium Development Goals (MDGs) (20). Donations of safe and effective drugs from pharmaceutical companies, adequate funds from foundations and bilateral donors to deliver these donated drugs, effective global health partnerships, effective systems of delivery, and good governance can help make these diseases history. For example, donated generic formulations of praziquantel from MedPharm and other groups were used in the Schistosomiasis Control Initiative and by African ministries to reduce the burden of urinary and intestinal schistosomiasis in school children in a number of African countries (20–22). The mass distribution of albendazole and mebendazole has lowered the disease burden of soil-transmitted helminths and consequently improved school performance in children (13). Dracunculiasis is poised to be eradicated (24).
To encourage product development by the private sector in LMICs, many high-income country governments offer incentives such as R&D grants, tax credits and priority regulatory review for orphan drugs. Orphan drugs are those developed for rare diseases that may be used to treat more prevalent conditions. For example, the drug compound cethromycin has been given orphan drug status and is being investigated as a prophylaxis against community-acquired pneumonia and the anthrax virus (15).

Initiatives such as advance market commitments, fast-track regulatory approval vouchers and humanitarian licensing practices have also been proposed to encourage product development. Funding agencies and private foundations now offer grants and prizes for innovative ideas and products. For example, The Bill & Melinda Gates Foundation’s Grand Challenges in Global Health programme targets 14 major global health challenges, with the aim of engaging creative minds across scientific disciplines to work on solutions that could lead to breakthrough advances in health. The resulting research outcomes could potentially have highly beneficial effects on the treatment and spread of infectious diseases.

Innovative mechanisms to finance the creation and delivery of new drugs for infectious diseases are also being developed. For example, GAVI Alliance offers advance market commitment to expedite the introduction of new vaccines by providing guarantees of the quantity and the purchase price of a vaccine once it enters the market.

The global health community needs to observe closely the impact of these partnerships and incentives on developing country innovation systems. Numerous partnerships and initiatives are being orchestrated but we know little of how these initiatives interact and overlap, the unwanted side-effects created, or how negative reactions are managed. To date, we have still not identified the most effective partnerships to encourage health innovation for the poor and there are few initiatives to develop or strengthen such partnerships in poor countries.

Funding for innovation – food for brains

The Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property (GSPOA), published by WHO in 2008, called for the need to promote new thinking on innovation and access to medicines and to develop capacity in relation to health innovation as an essential response to public health needs. The GSPOA specifically drew attention to the need to invest in science and technology research and capacity, local production of pharmaceuticals, clinical trials, regulation, intellectual property and traditional medicine (16). This requires commitment and know-how from stakeholders in high-income countries, as well as stronger commitment from stakeholders in LMICs. But what role should LMICs take in funding these types of health innovation? As discussed later in Chapter 5, most of these countries allocate relatively low percentages of their gross expenditure to R&D for health (5, 17).
To date, bilateral funding from high-income countries to low-income countries remains the main mechanism for improving access to health products for the poor. The US President’s Emergency Plan for AIDS Relief (PEPFAR) and the President’s Malaria Initiatives are two of the largest bilateral aid initiatives presently available.

Funds are also available through public–private schemes. For example, UNITAID – supported by a tax on airline tickets, by 29 individual countries and the Bill & Melinda Gates Foundation – functions as a central procurement agency for drugs to treat HIV infection, TB and malaria in LMICs. The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund) also provides financial aid to deliver treatment and prevention products for these highly prevalent infections. While most of these funds derive from government donations, UNITAID, Global Fund and partners have also implemented several initiatives to raise social awareness of these diseases and to solicit additional monies from private philanthropists: an example is the (RED)™ campaign and the Dow Jones Global Fund 50 Index (18). Though these schemes focus on the “big three” (HIV/AIDS, TB and malaria) infectious diseases, they illustrate what could be possible if similar approaches were applied to other infectious diseases of poverty.

The GAVI Alliance, MMV, DNDi and similar initiatives also have a significant portion (25.6%) of the total global funding for neglected diseases and have been successful in establishing a solid pipeline of more than 140 products (19). While these partnerships capture the imagination of donors and foundations, they do not necessarily address core health concerns in LMICs. Further, the initiatives do not always clarify the responsibilities of these countries or facilitate the development of their innovation capacities.

While...partnerships capture the imagination of donors and foundations, they do not necessarily address core health concerns in LMICs. Further, the initiatives do not always clarify the responsibilities of these countries or facilitate the development of their innovation capacities.

**CASE STUDY 4.2**

**Lessons from Cuba**

Cuba is a positive example of how initial public investments in pharmaceutical research and production capacity can be leveraged into developing country collaborations, the export of novel health products and the creation of a global health success story. Cuba’s state-run pharmaceutical industry was established in 1972 to import pharmaceuticals and export traditional medicines cited on the WHO Model List of Essential Medicines. By 1993, Cuba had reduced the importation of finished medicines and instead was producing its own pharmaceutical products. This included over 1000 biologic and diagnostic products, as well as 162 non-prescription and generic drugs. Strong and enduring collaborations between national scientific and public health institutions led to the development and production of 11 vaccines, including the Cuban meningococcal BC vaccine, Haemophilus influenza type B vaccine, immunodiagnostics systems and more than 40 therapeutic products including monoclonal antibodies and recombinant proteins and drugs for HIV/AIDS. While Cuba imports most of its raw pharmaceutical materials from countries such as China, it exports not only pharmaceuticals but also health education, health promotion and methods of product delivery to low-resource settings in Africa, Asia and Latin America (20–22).
Despite the work of organizations including WHO/TDR, product-focused initiatives remain concentrated in developed nations and LMICs have not been able to take full advantage of them. In instances when agencies designate funds for in-country operational research, technical expertise and technology is often lacking and so funds are quickly diverted. Investment in product-focused research needs to be matched with investment in health systems, good governance and other structures to create and strengthen the innovation systems in LMICs (see Case study 4.2 opposite).

**Priority setting for health R&D – where to start?**

To invest effectively and strategically in R&D, funding agencies need to move away from disease-specific approaches, and think more broadly and systemically. The development of tools for disease prevention and control must take into account the changing global health context including the epidemiology and economics of disease, the increasing impact of climate change, and demographic changes including migration on disease distribution (see Chapter 2). Changing health systems and structures, and the values that underpin these, need to be accommodated (Chapter 3).

As noted above, considerable political and funding support has been directed to HIV/AIDS, TB and malaria, but little attention has been paid to other “neglected” infectious diseases, despite the fact that infections such as intestinal helminths and schistosomiasis are frequently co-endemic with malaria and HIV/AIDS (23, 24). Delivering rapid-impact drug packages could have important preventive and collateral effects, including reducing disabilities, improving well-being and, in some instances, disrupting disease transmission (25). Such a single dose of combination drugs not only addresses the need to treat common coinfections, but also saves time and reduces the direct and indirect costs for both health provider and consumer. Women – who are most often the community health providers as well as the ones responsible for household health care needs – are especially advantaged by this approach. Priority needs to be given to develop tools which are effective and affordable, have high benefit–cost ratio, are sustainable and carry low risks. They need also to be culturally appropriate and acceptable.
Policy environments in developing countries – more than scaffolding required

Effective policy design and implementation are pivotal to supporting innovation and nurturing local industry (30–32). Countries such as Brazil, China, India and South Africa illustrate how national innovation policies and investment in science and technology infrastructure have resulted in improvements in public health. Different approaches have been followed: Brazil passed the Law on Innovation which strongly encouraged PPPs (33); China prioritized biopharmaceuticals and the modernization of traditional Chinese medicines (34); and South Africa created Biotechnology Regional Innovation Centres to identify and develop commercial opportunities in biotech (35, 36) (for India see Case study 4.3).

Although very different in culture, governance and policy, these innovative developing countries have commonalities that are pivotal to nurturing innovation. Foremost, they are relatively stable countries which have benefited economically from globalization. They have created local private sectors in health R&D, provided incentives for PPPs and encouraged technology transfers. They have designed innovative intellectual property management strategies through humanitarian licensing agreements, which have allowed for the manufacture of licensed products to promote the access of health technology in other developing countries.

Market and profit-driven private sectors in these countries service large domestic and international markets. Investments continue into science and technology infrastructure to resolve local problems. The potential of large populations as talent pools for professionals and entrepreneurs is increasingly being realized. By generating an environment that enables private initiatives to thrive, many developing countries (including China, India, Republic of Korea and Taiwan) have been able to maintain their talent pool, while also attracting returnees from the United States of America and the European Union who have much needed managerial experience, technical expertise and access to a global business network (30–32).

Investing in health R&D has provided social and economic returns, through direct-cost saving from using locally produced technologies and revenue generated from exporting products and services (31, 32). One indicator for the return on this R&D investment is the number of American pharmaceutical patents measured against gross domestic product per capita. India (3rd), China (4th), Brazil (12th) and South Africa (14th) are among the world’s top ranking for this indicator (5). Argentina, Indonesia, Malaysia, Mexico and Thailand are in the top 25 (40).

CASE STUDY 4.3

India, trade-related aspects of intellectual property rights (TRIPS) and the Patents Act

In India, the original Patents Act (1970) restricted patents on food, chemicals and drugs and discouraged the presence of multinational drug companies. This allowed local companies to build expertise in generic drug manufacturing and to sell drugs at low cost (37). On joining the World Trade Organization in 1995, India was required to comply with TRIPS. This could have reduced India’s generic drug manufacturing capacity and the availability of affordable essential medicines (38, 39). However, TRIPS was implemented judiciously and the Patents (Amendment) Act (2005) contained stringent intellectual property measures, opposition measures for challenging frivolous patents, limited patentability exceptions and detailed criteria for provisions relating to compulsory licensing and parallel importation (37). These legislative measures helped Indian companies to expand into foreign markets in the United States of America and Europe, and to offer the United States of America’s Food and Drug Administration approved facilities for drug R&D, including clinical trials, in India (37).
Other LMICs are seeking to emulate these approaches. Because they lack the capacity to innovate in all aspects of health, smaller countries have sought to invest strategically in particular areas. For example, Guinea-Bissau has started to formulate a national health research policy and build a functional system for health research; Mauritius has opted to build on its capacity for clinical trials; and Tunisia has identified particular aspects of pharmaceutical innovation to increase its capacity to produce essential medicines locally (41).

Established innovative developing countries such as Brazil, China, India and South Africa are well positioned to help other LMICs to innovate strategically. They share a similar burden of disease and have first-hand knowledge of the devastating effects of infectious diseases. Already these nations play a strong role in supporting global health research and innovation via their financial commitments, product, technology, and knowledge transfers. For example, Brazil’s Ministry of

**Public–private product development partnerships – the fast-track alliance**

Innovations in research management and financing have led to the formation of PPPs and product development partnerships (PDPs). The aim is to accelerate R&D, infusing business philosophies with values of social justice and equity to improve implementation and access to existing technology. PDPs can establish mechanisms to redistribute funds and pool expertise and, importantly, to share benefits and risks of investments in health R&D.

An increasing number of products are being developed and marketed by emerging economies with sustainable research and manufacturing capacity such as China, Brazil and India. Today, nearly 62 products (vaccines, diagnostics and drugs) are being developed by 78 companies in developing countries (42). These include innovative processes for manufacturing local versions of the recombinant hepatitis B vaccine in Cuba, India and the Republic of Korea; Brazil’s efforts to produce low-cost generic antiretrovirals for HIV/AIDS in order to provide free access to lifesaving drugs; and the development of the antimalarial arteether (a synthetic version of artemisinin) by India’s Central Drug Research Institute (40).

Pharmaceutical companies and global health programmes have also partnered with local research institutes to develop and manufacture new products. For example, arteether was transferred to Themis Chemicals Ltd. for commercial manufacture and distribution and is now sold in 48 countries (40); Fiocruz/Bio-Manguinhos and the Butantan Institute in Brazil have partnered with the HHVI, while Ranbaxy Laboratories Ltd. and Bharat Biotech International Ltd. in India are linked with the PATH Malaria Vaccine Initiative (40, 43). Such partnerships go beyond drug development and include drug manufacture – China is currently the leading global producer of penicillin, the Serum Institute of India Ltd. leads the production of the diphtheria-pertussis-tetanus

**Research Question:**

What policies, scientific and financial links should innovative developing countries mobilize in order to support health innovation systems in other LMICs?
vaccine, and over 60% of the United Nations Children’s Fund’s (UNICEF’s) vaccine requirements are met by Brazil, Cuba, India and Indonesia (31, 40).

The successes of public–private PDPs highlight the need to expand the scale and scope of activities. Until now, the focus typically has been on delivering a product or service for a particular disease within a specific timeline of five to ten years. The expectation of such short-term returns on investment has excluded LMIC partners with incipient research capacity but less experience with product development. This approach has also excluded embryonic technologies which require investment in R&D beyond the ten-year mark. To ensure long-term sustainable global health innovation systems it is important that LMICs with developing capacities be given more active roles in public–private PDPs. Innovation must include long-term capacity building as well as capitalizing on quick short-term gains.

Few PPPs and PDPs concentrate on the delivery and uptake of products or on strengthening local capacity for R&D. Innovations and partnerships to address these aspects of the system are important to ensure that innovations reach those who need them most. For example, PATH, an international non-profit organization, aims to advance relevant and appropriate health technology, strengthen health systems and encourage positive health behaviours in low-resource settings (44). The European and Developing Countries Clinical Trials Partnership (EDCTP) comprises 14 European Union Member States, Norway, Switzerland and 47 sub-Saharan African countries. It was established to accelerate the development of new pharmaceutical products through multi-centre projects by combining clinical trials with capacity building and strengthening of regional partnerships (45). More initiatives like these are required.

Social innovations – science on its own is not enough

Initiatives to strengthen health innovation systems must account for the complex challenges of health infrastructure, economics, social and cultural factors that inhibit people from accessing new and life-saving innovations. Innovation must include R&D and delivery. It is crucial to understand local contexts, engage communities and incorporate the wisdoms of local knowledge.

Partnerships between private, civic and public sectors should be strengthened to enhance access to essential drugs. Already, a number of partnerships have proven that success is possible. For example, in partnership with WHO, Merck & Co. and the Global Alliance to Eliminate Lymphatic Filariasis (GAELF), GlaxoSmithKline donated albendazole to mass-drug administration regimens of diethylcarbamazine or ivermectin. This has resulted in the near elimination of lymphatic filariasis in Egypt, Samoa, and Zanzibar in the United Republic of Tanzania (46–48). Pfizer worked through the International Trachoma Initiative to donate azithromycin and as a result, trachoma has virtually disappeared as a public health problem in Morocco (49, 50). Since the 1980s, Merck & Co. has donated over 300 million treatments of ivermectin for the control of onchocerciasis via the Mectizan® Donation Program in Africa and Latin America. This partnership has been running for 25 years and has proven so successful that it has been hailed as one of the greatest medical achievements of the 20th century (51–53).

1 For more information see (http://www.edctp.org/, accessed 1 March 2012)
OVERCOMING SOCIAL AND CULTURAL BARRIERS – GETTING COMMUNITIES INVOLVED

To expand access to health innovation, we must also factor in social and cultural barriers to prevention and care. These are associated with social norms, sex and gender biases, stigma and taboo behaviours. Too often interventions and innovations are not taken up because local communities are not consulted. The story of polio teaches us important lessons: the failure to obtain informed consent from parents of vaccinated children, combined with lack of clear communication about the limitations of the oral polio vaccine and the outcomes of vaccine-induced harm, have seen polio eradication campaigns beset by rumours, low attendance and active community resistance (54, 55). Instead of being eradicated years ago, poliomyelitis continues to affect people in LMICs. Similar themes have recurred in relation to other infectious diseases such as leprosy, leishmaniasis, Buruli ulcer, severe acute respiratory syndrome (SARS) and schistosomiasis (53).

Stigma often disproportionately affects women, resulting in delayed diagnosis; non-adherence to treatment; and greater psychological, social and emotional distress because of abuse, abandonment, divorce and other relationship problems (56, 57). In Ghana less than one quarter of people with schistosomiasis-related symptoms seek medical treatments through the health system (58, 59).

We need to find new ways of engaging communities so that initiatives are sustainable in the long term and not simply imported interventions, the effects of which will fade once the programme has ceased.

RESEARCH QUESTION:
What strategies and social entrepreneurship models are available for local communities to innovate in the prevention, control and treatment of infectious diseases?

CASE STUDY 4.4

The community-directed treatment approach

The community-directed treatment (CDT) approach has been implemented across 50,000 communities in Africa and is one of the most successful innovations in creating community ownership and building programme sustainability. Communities in meso or hyper-endemic infectious disease areas identify amongst themselves those who will be responsible for community-directed drug distributions, organizing distribution according to their own cultural norms and organizational structures. This approach builds programme sustainability, community ownership and empowerment. Cost-savings are made by health departments as staff do not have to be sent into the field to supervise distribution (60). CDT has been successfully implemented across 19 countries involved in the African Programme for Onchocerciasis Control (61). It has also been used in the control of lymphatic filariasis in Ghana (62), to distribute Vitamin A and iron supplements to nomadic pastoralists in western Kenya (63), and to teach Ethiopian mothers how to recognize and quickly treat children showing symptoms of malaria.
To overcome such barriers, we need to find innovative methods to translate and customize health interventions and products to local settings. In other words, we need to find new ways of engaging communities so that these initiatives are sustainable in the long term and not simply imported interventions, the effects of which will fade once the programme has ceased (see Case study 4.4).

**Building capacity – incubating entrepreneurship**

Capacity building is crucial if developing countries are to become active participants in innovation and research. Considerable efforts have already been made. WHO/TDR, the Wellcome Trust, Fogarty International Center, Japan Society for the Promotion of Science and the Academy of Sciences for the Developing World are among the agencies that have made substantial investments in human capital development in LMICs through scholarships and research training, institutional support and research project support.

Capacity building through the creation of centres of excellence has been successful in helping poorer countries to conduct high-quality research and produce new graduates, but the impacts are often localized to one or a few academic institutions. Despite active research programmes in infectious diseases, academic centres of excellence in most LMICs have been underrepresented in the various PPPs and PDPs whose initiatives drive the development of new health products. Rather than shaping the local culture of innovation, these centres of excellence can bias the national science and technology landscape as they have competitive advantage over local institutions for the limited human and financial resources for R&D. These centres are also more likely to have research collaborations with developed-country partners than in-country or regional partners. These partnerships are usually the results of engagement between individual researchers of similar research interests and technical expertise, which may not be conducive for interdisciplinary research towards innovative solutions. The performance of these centres must be continually monitored and evaluated to ensure their capacity in research innovation.

Many developing countries have also experienced a profound loss of human resources, not only in the R&D sectors but also across disciplines relevant to population health and disease control and in the health services system. Generations of young scientists, medical and public health professionals have been sent abroad for training. Often they continue to work overseas – in facilities with resources that cannot be matched in their poorer home countries. Talented individuals who have returned tend to be concentrated in the few centres of excellence where the research environment is most conducive for career development, or are diverted into senior administrative and management positions. They are liable to be cut off from the rest of the health infrastructure in these countries, so there is a need to better connect individuals at these centres with the rest of the health infrastructure in LMICs.

Areas of research such as the social sciences, epidemiology, and health systems research require significant local involvement in capacity training (see for example Case study 4.5). This is because the effective implementation and adoption of health solutions require understanding of local contexts and the participation of the local partners.
Innovative ways of capacity building need to be expanded, along with enabling environments to retain the talent pools. Interactive video and online training modules can be incorporated in training programmes and made accessible to researchers across countries through knowledge-sharing platforms such as the WHO/TDR TropIKA.net portal (65).

Mechanisms to promote R&D spin-offs from academic institutions in developing countries also require personnel with research management skills. Without individuals with “technopreneurship” or private sector experience to support local academic scientists, R&D spin-off projects may suffer from a higher than necessary attrition rate and lower returns on investments.

**Ethics, innovation and infectious disease**

Science cannot be an end in itself; it needs to be framed by moral and ethical imperatives. Innovation must start with the premise that the ultimate aim is to reduce health inequities.

Rapid shifts in technology and policy can have detrimental effects on human health, cultures and the environment. Critical reflection is needed on how new science influences the biosphere; how medical interventions affect the quality and dignity of human life; and how discrepancies in power and knowledge may be used to subjugate others (66). On one hand, the pharmaceutical industry has become a close partner with public health initiatives, particularly in dispersing essential drugs and medicines to LMICs. On the other hand, vulnerable people continue to be recruited into clinical trials, in environments that are poorly regulated, where ethics and the rule of law are not easily enforced (67). The enthusiasm of some LMICs to establish themselves as hubs for clinical trials and drug development needs to be tempered with concerns over their regulatory capacity to cope with the influx of trials, limited ethical oversight and the impact of poorly designed and implemented trials on human subjects.

**Case Study 4.5**

Consortium for Advanced Research Training in Africa (CARTA)

CARTA (64) is an innovative capacity-building initiative in public health and the social sciences. It aims to train African researchers at their own universities, while building a critical mass to sustain Africa’s strongest and most talented researchers. CARTA involves nine academic and four research institutions from west, east, central and southern Africa, to provide doctoral training in population and public health and strengthen research infrastructure and multidisciplinary research capacity. CARTA Fellows enrol in a PhD degree programme in a member university and are supervised by African researchers. They participate in extended residential seminars at key points during their doctorates, facilitated by senior staff from both African participant universities and research institutes, and select “northern” partners including WHO/TDR. These seminars offer training in research methods, disciplines and theories relevant to population health, and generic teaching, research management and grants skills. Training opportunities are also provided for their supervisors to gain new and upgrade existing skills, and to take advantage of expanding research networks. The African-led nature of CARTA ensures sustainable, measurable changes in research capacity, output and translation of population and public health.

**Research Question:**

What is the most effective way to link the local milieu of innovation in the public and private sectors in LMICs with international partners?
Further, the pursuit of innovation cannot displace the need to address weak infrastructure and inequities. Nor should the pursuit of the “new” and relatively untested replace what has been shown to work. Occasionally, new practices have been employed, without evidence to prove their efficacy. This poses risks to patient safety and quality of care. In other cases, what has been proven to work is not disseminated throughout health systems (68). Sound science requires continuous evaluation and assessment to determine a rigorous evidence-base and the feasibility and transferability of an initiative (69).

Too often, innovation has concentrated on expensive and complex technological interventions, difficult to implement in developing country settings and available only to a privileged few. Understanding of the local context is critical, especially in impoverished communities; companies must consider how power and conflict affect the health of the most vulnerable. Ultimately innovation is not just doing things differently but doing things more safely, more effectively and more equitably. This might mean starting in settings in which poor people are already engaged. This is likely to include informal, unregulated providers; local associations such as citizen groups; and engagement with local governance where structures and accountability mechanisms are not always transparent (17). A democratic and grass-roots approach is essential but raises challenges such as managing competing interests, waning commitment and mitigating the unforeseen effects of the innovation itself (68).

A three-step approach to future research

To alleviate the effects of infectious diseases, especially on our poorest and most vulnerable, we need to engage with all aspects of the innovation system. Different sectors and systems for innovation need to integrate with one another to address the dynamic interaction of social, ecological and biological factors that influence the prevalence of infectious disease. Only by doing so can the development and delivery of relevant, appropriate and effective innovation and technologies be accelerated. We argue that there are three essential approaches:

1. to develop more open models of sharing new knowledge and products
2. to highlight the importance of innovation by engaging key players in global networks
3. to work towards a “one world–one research” community agenda.

Ultimately innovation is not just doing things differently but doing things more safely, more effectively and more equitably.
NEW MODELS OF SHARING AND DELIVERY – THINKING OUT OF THE BOX

Research is needed to determine the best models for sharing of knowledge and delivery of new innovations. Drug and product development are long and expensive processes – relying solely on philanthropic donations to support these endeavours is not sustainable. There have been calls for an open-access approach to innovation and drug development (70), i.e. closer interactions between academia, biotechnology and the pharmaceutical industry to improve productivity through pre-competitive collaboration (71). Open-access models already exist. GlaxoSmithKline established the Tres Cantos Open Lab Foundation in Spain, focusing on TB, malaria and trypanosomiasis. Scientists from around the world can come together to collaborate and share intellectual property in relation to these infectious diseases. GlaxoSmithKline has also made 13,500 malaria compounds from its private library publicly and freely available in the hope that new medicines for malaria can be developed. A similar initiative is underway in Singapore at the Novartis Institute for Tropical Diseases, with special emphasis on dengue, TB and malaria.

These efforts need to be scaled-up. Existing financial constraints can dampen R&D efforts and it is important that resources be maximized. A culture of open innovation is crucial to share knowledge, technology and repositories, particularly in the current financial climate. Repositories may include demographic and biological databases (see Case study 4.6); bio-banks (e.g. cell lines, reference samples, microorganisms, bioreagents); biomarker banks (e.g. DNA, single nucleotide polymorphisms, proteins); standards libraries for common testing and validation; and compound libraries. Repositories should also include databases for traditional knowledge; social science data; archives protecting indigenous intellectual property; and platforms documenting health and social innovations (72).

Policy reform is necessary to create an open innovation platform. Most importantly, a global commitment is needed to develop sophisticated regulatory and intellectual policies to provide the framework for manufacturers to produce high quality products and sustain their competitiveness in the globalized marketplace. A recent initiative by

CASE STUDY 4.6

Knowledge sharing to control soil-transmitted helminths and schistosomes in sub-Saharan Africa

An open-access knowledge management platform has been established to document the prevalence of soil-transmitted helminths and schistosomes for the whole of sub-Saharan Africa (73). In recent years, geographical information systems technologies, global positioning systems in field surveys and the increased availability of online electronic gazetteers have expanded the project with geo-position survey data at actual location. These data provide essential information for control programmes and for the research community to know where and when to target control and treatment initiatives for helminth infections in sub-Saharan Africa.
Chapter 4

Global Report for Research on Infectious Diseases of Poverty

110

INNOVATION AND NEW TECHNOLOGIES TO TACKLE INFECTIOUS DISEASES OF POVERTY

Innovation and new technologies to tackle infectious diseases of poverty

Fig. 4.2. From technology platform towards innovations. Open innovation platform as a mechanism for driving and supporting “home grown” innovations in low and middle-income countries.

the World Intellectual Property Organization, WHO and the World Trade Organization aims to improve access to patent information for public health and access to medicine, and freedom to operate with the help of a user-friendly database that contains public information on health-related patents (74).

A culture of innovation needs to be created in the workplace, among governments and researchers. Complementary platforms and an open-innovation environment are necessary for exchange of resources, information and human capital.

BUILDING NETWORKS AND AN INNOVATION PLATFORM – TYING KNOTS THAT WILL HOLD

Because health encompasses both the physical and mental well-being of an individual – and is influenced by many social, economic, environmental and biological factors – an investment in health services alone is insufficient to maintain a nation’s health and competitiveness in the globalized world. Investment in a responsive health innovation system needs to be an integral part of the national innovation system, and should translate across organization levels and government sectors to respond adequately to local, as well as cross-border, health issues.

Addressing the complexity of infectious diseases of poverty and reducing the gap in health inequalities will require breaking down the silos of traditional research and funding programmes. New innovations
focusing on cross-cutting platform technologies will need to be fostered so as to achieve synergy between programmes and sectors at the local and regional levels. An open innovation environment is necessary for this to occur (see Fig. 4.2), where information and resources can be shared and complementary platforms of technology can be applied to find the best solutions in local contexts where infectious diseases and poverty are co-endemic.

Basic and translational research activities conducted through shared research and technology platforms may result in spin-offs in product development and health services, in new approaches to disease control, or in new mechanisms for delivering health services. To achieve sustainable results, these technology platforms should be regionally based to support local R&D. A culture of innovation needs to be created in the workplace, among governments and researchers. Complementary platforms and an open-innovation environment are necessary for exchange of resources, information and human capital.

An open innovation platform should bring together independent but cooperating agencies and consortia (75). Networks of researchers, community members and health workers can help progress research; monitor health indices; undertake community audits and evaluation; better manage intellectual property; and distribute financing. With the increase in large-scale drug-based multidisease control programmes, there is a need to monitor pharmacological side effects and community attitudes towards health technologies and to strengthen capability to translate technologies into local solutions. New approaches to partnership can capitalize on local skills and create larger markets. Significant LMIC participation in these networks, beyond a simple transfer of tools from innovating countries to LMICs, is essential. Genuine efforts to build capacity will increase the suitability, uptake and sustainability of health innovations. It will ensure greater return on initial investments by donors or multinational companies and enable the development of necessary expertise and “home-grown” solutions for infectious disease control. Increasing the capacity of LMICs is important to changing the research paradigm: from how and where products are developed, to changing disease priorities and the organization of funding.

Existing regional networks have been established but are in their formative stages. Launched in 2010, the African Network for Drugs and Diagnostics Innovation seeks to strengthen national capacity by building regional networks to address local health needs. Other such networks include the Association of Southeast Asian Nations Regional Network for Innovation and the Network for Drugs and Diagnostics Innovation in China, India and Latin America.

Criteria to guide the efforts of LMICs in aligning local or regional needs for infectious diseases with the technology platform needed to deliver appropriate solutions should include:

- relevance of the diseases and technology in the context of LMICs
- potential for implementation in the LMICs
- sustainability of the proposed measures
- potential for value chain creation across health sectors
- potential to strengthen networks of LMICs
- commitment of LMICs, along with enabling policies and earmarked budget
- external support and commitment of international stakeholders to support and assist LMICs.
**CASE STUDY 4.7**

**Suppressing dengue transmission in Aedes populations**

Recently, researchers in the United States of America and Australia successfully managed to introduce the intracellular bacterium Wolbachia into wild mosquito populations of *Aedes aegypti*, the dengue vector. This interfered with the reproductive capacities of the mosquitoes, the transmission of the dengue virus and the lifespan of the mosquito. The Wolbachia-carrying mosquitoes were released in two suburbs in Cairns, Australia. Prior to release the researchers undertook strong community engagement to garner community support and also sought appropriate regulatory approval from the Australian Pesticides and Veterinary Medicines Authority. Results from this study show that, by protecting mosquitoes from transmitting dengue fever, it might be possible to prevent the 50 million human cases of the disease reported every year. Further trials are planned to be undertaken in Brazil, Indonesia, Thailand and Viet Nam.

*Source: Reference (80)*

---

**INNOVATING FOR “ONE WORLD, ONE HEALTH” – ONE PHRASE SAYS IT ALL**

Health innovation is only possible with interdisciplinary learning and integrated delivery with other programmes. In an increasingly interconnected world many factors – social, economic, environment and biology – influence an individual’s health. Investing in health innovations without incorporating the broader determinants of health will not be sufficient to maintain a nation’s health and R&D competitiveness.

Instead, we need investment that fosters interdisciplinary collaboration; integration of health innovation within national innovation systems; and products and tools which are translatable across government sectors and organization levels. Focusing on cross-cutting technological platforms – such as fermentation technology, clinical trials capacity, information and communication technology, and wireless communication for operation and field research – increases the likelihood of developing innovations for the control and prevention of multiple diseases appropriate for the community in the local context.

The “One World, One Health” approach (see Chapter 2) presents an important lens through which policy-makers, funders and the academic community must view infectious diseases of poverty (76). There is an inextricable link between human–animal health and the environment. Exciting possibilities for innovation exist at this interface (see Case study 4.7). For example, genomic tools can be used to quickly identify and understand newly emerging viruses, their mutations, interactions with other receptors and replication in their hosts. Such analysis could enhance our understanding of how different host pathways affect the outcome of zoonotic transmission (77). Plant-derived pharmaceutical proteins can offer new products for the treatment of diseases. Examples

*“If we are serious about innovating to address infectious diseases of poverty, we need an innovative system with a focus beyond product development.”*
of proteins closest to commercialization include the hepatitis B virus surface antigen (hepatitis b), Lactoferrin (gastrointestinal infections), and rabies glycoprotein (for rabies) (78). Plant molecular farming has the potential to yield higher agricultural outputs as well as maximizing the yield of recombinant proteins in seeds; such studies have important implications for enhancing human health and developing new treatments for disease (79).

**Conclusion – innovate or fail**

If we are serious about innovating to address infectious diseases of poverty, we need an innovative system with a focus beyond product development. This system needs to be able to respond to changing global health needs, translate technological development, deliver useful innovation and, eventually, ensure greater sustainability and equity for the world’s poorest populations.

LMICs must be actively involved in the health innovation system so that the tools and innovative approaches necessary to deal with infectious diseases are developed with significant participation of the countries affected by those diseases.

Disparate research capacities need to be brought together to consolidate and expand research and innovation in disease prevention, control and treatment. Enabling policies and mechanisms (i.e. harmonization of science, technology and innovation policies, intellectual property management, sustained financial commitment, incentives for intersectoral cooperations) are crucial to support R&D to enable significant innovations, attract partnerships with private sectors and help to reduce the investment risk for all stakeholders.

**RESEARCH QUESTION:**

*We need to better understand the "eco-social" factors which facilitate resistance. What strategies – biological, chemical, genetic, cultural and social – exist to better control pathogens and vectors?*

Innovation is not easy. It is complex, time-consuming work that requires global and local input, partnerships and collaborations, funding, enabling policies and long-term commitment. The rewards make it worthwhile to pursue: improvements in public health which took Europe 150 years to achieve in the 19th century were achieved by Latin America and east Asia in only four decades of the 20th century. This was due to significant human development and technological and medical interventions (15). In the 21st century, such achievements are possible globally.
Chapter 4

References – Chapter four


34. Pefile S et al. Innovation in developing countries to meet health needs: experiences of China, Brazil, South Africa and India. Geneva, World Health Organization, 2005 (CIPIH Study 10d [DGR]).
45. European and developing countries clinical trials partnership. The Hague, European and Developing Countries Clinical Trials Partnership (http://www.edctp.org/, accessed 18 February 2012).


Chapter 4

Global Report for Research on Infectious Diseases of Poverty


