Emerging innovation practices and policies for the health-care needs of resource-poor people

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The emerging innovation practices and policies for affordable global health solutions for resource-poor people are demonstrated with suitable examples, both illustrative and inspirational. It is concluded that innovation can indeed impact the entire chain of diagnosis, drug discovery, development and health-care delivery.

Introduction

Making better health-care accessible, affordable and available to resource-poor people is an urgent challenge[1]. Innovation will be the key in attaining these goals.

Innovation is required in the entire chain of diagnosis, discovery, development, health care delivery and even in financing[2,3,4]. The innovation challenge will be to get, as we shall show, “more from less for more”.

Discovery and development

Just a decade ago, the journey from the discovery of a new molecule to the marketplace used to take around 10 years and cost around US$ 250 million. Today, the same journey takes anywhere between 10 to 15 years and costs around US$ 1–1.5 billion. On the other hand, the Food and Drug Administration (FDA) approved only 21 new molecular entities as against around 30–40 a decade or so ago. In other words, we are getting “less for more for less” i.e. “fewer” molecules approved by the FDA, which are developed with much “higher” costs and taking a much “longer” time. This makes them less affordable, which means access of these therapeutics to a lesser number of patients. The challenge is to reverse the current trend of “less from more for less” to “more from less for more”, which means more (performance in terms of safety and efficacy) for less (cost of development) for more (resource-poor people).

Traditional or alternative medicine

Traditional or alternative medicine can offer accessible and affordable health care, especially for preventive medicine and chronic pathophysiological states. It can also serve as a rich knowledge resource for new drugs[5–8]. One promising approach is traditional knowledge-inspired reverse pharmacology[7], which reverses the routine “laboratory-to-clinic” process to “clinics-to-laboratories”.

Reverse pharmacology is a rigorous scientific approach to use the documented clinical experiences as well as qualitative experiences and observations for developing target candidates or formulations through robust preclinical and clinical research. In this process “safety” remains the most important starting point and “efficacy” becomes a matter of validation[7].

The Council of Scientific and Industrial Research of India, under the programme known as the New Millennium Indian Technology Leadership Initiative (NMITLI) invested in the reverse pharmacology approach through a partnership with industry and academia. The approach will be illustrated with a typical example of the development of a drug for psoriasis, which is presently in phase III clinical trials.

A leading Indian pharma company used an indigenous knowledge base of a practitioner in a village. It did rigorous scientific and clinical work to validate the claims. Thus extensive studies comprising fingerprinting, activity-guided fractionation, efficacy studies, toxicology, safety pharmacology, pharmacokinetics and toxicokinetics helped the company in filing an Investigational New Drug (IND) application. A single plant-based oral herbal formulation was developed, which has a novel mechanism of action with effective modulation, the cellular function leading to marked psoriatic lesion improvement without any toxic effects. The guidelines laid down by the US FDA for botanicals as well as Drugs Control General of India (DCGI) norms on new drug development were followed. The work is in phase III clinical trials and, if successful, will be introduced in the market by the end of 2010.

In this specific case, the contrast in terms of potential lowering of cost of treatment (about US$ 100 as against, say US$ 20 000 for antibody treatment), the time for development (six years as against the conventional 10–15 years) and cost of development (about US$ 10 million as against upwards of US$ 500 million) is evident[7].

Patwardhan and Mashelkar[7] have given other examples of reverse pharmacology. Several drugs for other diseases such as cancer, diabetes, osteoarthritis, hepatitis, etc. are at various stages of development through the reverse pharmacology route.

Open source discovery

The WHO Commission on Intellectual Property Rights, Innovation and Public Health, of which one of the authors

(RAM) was a Vice-Chair, made a recommendation in its 2006 report:

"Practical initiatives that would motivate more scientists to contribute to this field through "open source" methods should be supported."[1]

It was India's Council of Scientific and Industrial Research (CSIR) that made it into reality. It launched the first ever Open Source Drug Discovery (OSDD) consortium with global partnership with a vision to provide affordable health care to the developing world by providing a global platform[9].

OSDD is a concept to collaboratively aggregate the biological and genetic information available to scientists in order to use it to hasten the discovery of drugs. It incorporates a web-based platform for scientists and students all over the world to share research and collaborate on drug discovery projects for malaria, TB and other neglected diseases (www.osdd.net). One such project leveraged the world's largest Mycobacterium tuberculosis (MTB) database to bring together 13 researchers across India to decode 400 of the 4000 genes of MTB in less than six months[9].

The Government of India's commitment of US$ 38 million towards this project is being now followed with equivalent funding being raised from international agencies and philanthropists[10].

"Out of patent" based innovative drugs

Most of the "out of patent" existing therapeutics have not yet been fully optimized, which can be done by using innovative engineering approaches. This approach can offer potentially superior drugs at far cheaper prices.

In a recent study, bioengineers at MIT engineered a novel nanoparticle that could enable a rational combination of two drugs, where the sum of the effects was greater than the individual[11]. These could treat tumours more effectively than existing regimes and also reduce the side-effects.

Because researchers designed them using polymers and drugs that are already approved for human use, one can quickly move into clinical trials. Now at Harvard Medical School and Brigham and Women's Hospital, scientists are working on extending these concepts to treat other diseases.

In addition, these scientists are using cost-effective biocompatible nanomaterials such as carbon-derived fullerenols to change the pharmacokinetic and pharmacodynamice properties of existing therapeutic agents to increase the therapeutic index[12]. This has the potential to improve upon the efficacy and safety of "out of patent" drugs. Nanotechnology holds the potential to deliver the active agents specifically to the desired site of action, thus reducing the total drug requirement, and therefore reducing the cost.

Affordable diagnostics

Low-cost diagnostics for priority global health conditions is an initiative launched by the Bill & Melinda Gates Foundation (www.grandchallenges.org). Out-of-the-box thinking will be increasingly needed.

For instance, Whitesides and his group[13] have developed "paper based diagnostics", which can be used in villages. They have the advantage of not using any electronics and also surviving the harsh conditions of dust, humidity and extreme temperatures.

On the other end, advanced technologies can reduce the costs too. The possibility of resolving the sensitivity of detection using nanostructures, such as carbon nanotubes and nanocantilevers means that detecting a disease at an early stage is now a realistic goal. This can dramatically impact on the clinical outcome and reduce the burden on the health-care system[14].

Similarly, disposable "lab-on-a-chip" devices can enable rapid diagnostics at remote sites, which can enable effective disease management[15]. This can especially revolutionize the management of HIV, where delayed diagnostics can mean loss of contact with the patient, who in most cases, will not be able to afford a prolonged stay at the site of the health-care facility.

Innovations in delivery

Innovations in delivery are as critical. Recently, at the 6th Annual World Health Care Congress some interesting themes (http://www.worldcongress.com/events/HR09000/) were showcased as "Extremely Affordable Health Innovations"[16] with "extreme affordability" being demonstrated by the two examples listed below.

Incubator for US$ 25

Embrace is a nonprofit organization that aims to help the millions of vulnerable babies born every year in developing countries through a low-cost infant incubator. Unlike traditional incubators that cost up to US$ 20 000, the Embrace infant warmer costs US$ 25. The device requires no electricity, has no moving parts, is portable and is safe. Twenty million vulnerable babies born across the globe each year can be helped.

Cataract surgery for US$ 25

Aravind Eye Care System (AECS) has successfully developed and implemented a high-volume, high-quality, cost-effective eye care model and taken it to the doorstep of rural India[17].

With less than 1% of the country's ophthalmic manpower, AECS performs about 5% of all cataract surgeries in India. As a result of the unique work flows and fee system, AECS has become self-sustaining, treating over 1.4 million patients each year, two thirds of them for free. It works with more than 200 hospitals located all over India as well as in the developing world, helping them to replicate the Aravind model in these countries.

Innovations to reduce patent monopolies

When the market has very limited purchasing power, as is the case in developing countries, patents are not necessarily effective in stimulating research and development (R&D) and bringing new products to the market[18]. Many innovations have been suggested to address this challenge.

Patent Pools

A patent pool is a mechanism, whereby a number of patents held by different entities are made available to others for

production or further development. The patent holders receive royalties from the users.

Patent pools are part of World Health Organization's recently adopted Global Strategy on Public Health, Innovation and Intellectual Property to help increase access to medicines.

Several such initiatives are underway. For instance, Knowledge Ecology International (http://www.keionline.org/) is trying to create a patent pool for medicines in low- and middle-income countries. In February 2009, Glaxo Smith Kline (GSK) has announced a patent pool initiative, with the intention of putting many drug patents for tropical diseases into a free pool.

In July 2009, Alnylam Pharmaceuticals announced that it will contribute its RNAi technology patent estate and know-how to the GSK patent pool. GSK granted South Africa's Aspen the right to make its HIV drug abacavir in a royalty-free licensing deal, although HIV drugs have not so far been included in the patent pool. The year 2009 has thus seen progress[19].

Global Responsibility Licence

The proposed Global Responsibility Licence (GRL) is an approach with great potential[20]. GRL is envisaged to be a standard, global licence for patents, which allows public and not-for-profit research organizations to undertake research for "non-market uses". This licence would be used to help nonprofit organizations and research agencies improve the state of the world in very meaningful and practical ways.

GRL is different to a "patent-pool" approach in that it does not give ownership of the original IP away. Any firm retains control of its IP portfolio, but the transaction cost of licensing for philanthropic purposes is greatly reduced.

Other emerging innovations in practices and policies

Current health financing includes international health funds (e.g. the Global Alliance for Vaccines and Immunisation – GAVI), product development partnerships (e.g. IAVI, PATH), International Finance Facility for Immunization (IFFIm), Advance Purchase Commitment (Pneumococal Advance Purchase Commitment), UNITAID, etc[22]. We need to move beyond these.

Just as "outsourcing" has brought down the costs, so can innovative "crowdsourcing". In "crowdsourcing" an undefined large group of people takes on tasks usually performed by employees in response to an open call[23]. Innocentive, Ninesigma, Foldit, etc. are brilliant examples of crowdsourcing.

The current "push" and "pull" mechanisms work within the existing regimes of IP protection. However, rewarding innovation by offering prizes or compensation based on the extent of disease averted in developing countries is an interesting innovation[24,25].

Finally, the "grand challenges initiative" posed by the Bill & Melinda Gates Foundation (www.grandchallenges.org) is one of the most innovative ones in recent times. It is a five-year US$ 100 million initiative to encourage bold and unconventional research on novel global health solutions. It challenges the best minds around the world with a chance to win US$ 1 000 000 grants to further their research.

Key messages

- Innovation directed towards the goal of getting "more (performance) from less (cost) for more (people)" is needed.
- Innovation should be across the entire chain of diagnosis and discovery, development and delivery of therapeutics, diagnostics and vaccines.
- Innovative Developing Countries (IDCs) should play a greater role in developing innovative practices and policies for the health-care needs of resource-poor people.

Conclusion

The emerging innovation practices and policies for health care needs of resource-poor people must hinge around innovations that can get "more from less for more". The entire chain beginning with diagnosis of a disease, to discovery and development of a new therapeutic, to its delivery needs radical innovations. Some illustrative, but also highly inspirational examples, have been given to show how this can be achieved.

Finally, the growing ability of some developing countries like India, China, Brazil, etc. (also referred to as Innovative Developing Countries (IDCs)) to undertake health innovation is an increasingly important means to improve health equity[21]. Health innovation networks from such as IDCs should increasingly be used to help achieve the goal of "health for all and not a privileged few". ❑

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He is the cofounder of Cerulean Pharmaceuticals. Chosen as one of the top 35 innovators of the world under 35 years of age by Technology Review Magazine *(2005), Dr Sengupta received the Era of Hope Award (2007) and Innovator Collaborative Award (2009) from the US Department of Defense. He was a Nehru Scholar at Trinity College, University of Cambridge, and a fellow at the Massachusetts Institute of Technology (MIT).*

With the Department of Biotechnology, Government of India, he is establishing the Translation Health Sciences and Technology Institute in India.

References

1. Dreifuss R, Mashelkar RA et al. Public health, innovation and intellectual property rights. Report of the Commission on Intellectual Property Rights. World Health Organization, Geneva, 2006.
2. Widdus R, White K. Combating diseases associated with poverty: financing strategies for product development and the potential role of public-private partnerships, (www.mmv.org/IMG/pdf/Combatingpoverty/PPH.pdf), 2004.
3. Burke MA, Martin SA, eds. *Global Forum For Health Research: Monitoring financial flows for health research*, 2006.
4. Editorial, *Lancet*, 2004, 364:1555–1556.
5. Wonderling D et al. Cost effectiveness analysis of a randomized trial of acupuncture for chronic headache in primary care. *British Medical Journal*, 2004, 328:747–52.
6. Oz M. Emerging role of integrative medicine in cardiovascular disease. *Cardiovascular Reviews*, 2004, 12(2):120–123.
7. Patwardhan B, Mashelkar RA. Traditional medicine-inspired approaches to drug discovery: can Ayurveda show a way forward? *Drug Discovery Today*, 2009, 14(15/16), 811.
8. Padma TV. Ayurveda. *Nature*, 2005, 436, 486.
9. http://www.osdd.net
10. Kniaz S. The best thing to come out of India since “Slumdog Millionaire”. *Global Health Policy*, 11 March 2009.
11. Sengupta S et al. Novel cancer therapy through temporal targeting of both tumour cells and neovasculature using a unique nanoscale delivery system. *Nature*, 2005, 436:568–72.
12. Chaudhuri P et al., Fullerenol-cytotoxic conjugates for cancer chemotherapy. *ACS Nano*, 2009 (in press).
13. Andres W et al. Patterned paper as a platform for inexpensive, low-volume, portable bioassays. *Angewandte Chemie International Edition*, 2007, 46, 1318–1320.
14. Wang C, Madou M. From MEMS to NEMS with carbon. *Biosens Bioelectron*, 2005, Apr 15;20(10):2181–7.
15. Myers FB, Lee LP. Innovations in optical microfluidic technologies for point-of-care diagnostics. *Lab on a Chip*, 2008, Dec;8(12):2015-31.
16. Golden P. World Health Care Congress focuses on extremely affordable health innovations. *Medical News Today*, 16 March 2009, http://www.medicalnewstoday.com/articles/142318.php.
17. Tabin G. The Cataract Blindness Challenge Innovations Case Discussion: Aravind Eye Care System. *Innovations,* 2(4), 53–57 (doi:10.1162/itgg.2007.2.4.53).
18. Kaiser J. NIH to limit scope of foreign patents. *Science*, 2002, 296, 2316.
19. Bioventures for Global Health, 2009. www.bvgh.org, info@bvgh.org
20. http://www.weforum.org/pdf/YGL/editorials/moody.pdf.
21. Morel CM, Acharya T, Broun D et al. Health innovation networks to help developing countries address neglected diseases. *Science*, 2005, 309, 401–404.
22. IAVI insights. Innovative financing mechanisms to advance global health. Policy Brief 21, 2009.
23. IAVI Report. Crowdsourcing vaccine challenges, 2009, www.iavireport.org.
24. Nathan C. Aligning pharmaceutical innovation with medical need, *Nature Medicine*, 2007, 13, 3004–3008.
25. Love J. World cash prizes promote cheap drugs, 2007, http://www.newscientist.com/article/mg19626296.