

In Search of New Ideas for Global Health

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The recent failure of another potential vaccine against human immunodeficiency virus (HIV) underscores the enormous challenges of tackling diseases whose heaviest burden falls on the developing world. A quarter of a century after the first report of AIDS, our knowledge about how an HIV vaccine might work is still distressingly limited. It seems clear that neither current dogma nor traditional thinking is likely to get us to the next step. Truly creative ideas will be required.

I must confess to having learned the hard way that embracing new thinking, as difficult as it may be, is crucial for the advancement of science and medicine. As a gastroenterologist, I was one of the many who believed as gospel truth that peptic ulcers were caused by gastric acid. When two scientists from Australia came along and argued that it was actually a bacterium, *Helicobacter pylori*, that produced ulcers, those of us in the “Acid Mafia” rejected their claims out of hand. But Robin Warren and Barry Marshall persisted. Marshall even drank a solution of *H. pylori*, became ill, took antibiotics, recovered, and wrote a paper about it, just to get others in the field to pay attention. You know the ending to this story — these scientists were proved right and went on to win a Nobel Prize in 2005.

New ideas should not have to battle so hard for oxygen. Unfortunately, they must often do so. Even if we recognize the need to embrace new thinking — because one never knows when a totally

radical idea can help us tackle a problem from a completely different angle — it takes humility to let go of old concepts and familiar methods. We have seemed to lack such humility in the field of global health, where the projects related to diseases, such as HIV, malaria, and tuberculosis, that get the most funding tend to reflect consensus views, avoid controversy, and have a high probability of success, if “success” is defined as the production of a meaningful but limited increase in knowledge. As a result, we gamble that a relatively small number of ideas will solve the world’s greatest global health challenges. That’s not a bet we can afford to continue making for much longer.

Incremental innovation has its place, of course. Many important lifesaving advances have been made by taking one crucial step forward at a time. Consider the worldwide effort to eradicate polio, for example. In 1955, Jonas Salk’s vaccine showed that we could induce protective immunity against poliovirus by injecting people with inactivated viral strains. Because his vaccine required injections, it wasn’t well suited to use in developing countries, but Albert Sabin’s oral polio vaccine took us a step further and allowed the first global eradication campaigns to begin. Both Salk’s and Sabin’s solutions, however, would have been impossible had it not been for a great leap — an essentially transformative idea — that had occurred centuries earlier in the mind of Edward

Jenner, who observed that milkmaids who had been exposed to cowpox became immune to smallpox, a far more deadly disease.

How can we capture such transformative innovation in order to address the problems in global health? First, it is clear that innovation does not take place only in the United States or Western Europe. In the realm of information technology, for example, many of the most important recent advances have been made in India or China. Innovation comes from every discipline. If only the anointed experts are permitted to address a problem, their field becomes locked in unchallenged dogma. An engineer or a physicist could have brilliant insights into a difficult biomedical problem. Innovative ideas might exist in the minds of people who could never navigate their way through a grant application for the National Institutes of Health. Moreover, new ideas can be fleeting, and waiting a year for funding in order to test them can have a serious dampening effect. Innovation frequently arises from the lessons of repeated failure, so if we are not willing to take risks and fail often, we will miss many opportunities to capture novel approaches that can transform a field. Above all, unfortunately, peer review can kill truly novel ideas because they are, by definition, peerless.

To help promote a more adventurous approach to research, the Bill and Melinda Gates Foundation, where I am president of the Global Health Program, is

willing to take risks as well. We are launching a \$100 million initiative called Grand Challenges Explorations, which will supplement our current grant making by funding hundreds of innovative early-stage projects over the course of 5 years, investing \$100,000 in each one. We want bold ideas — even seemingly wacky ones — that need just a little help to get tested. Proposals will require creative thinking but no preliminary data. The applications are only two pages long, and we'll make a funding decision within about 3 months after the May 30 submission deadline. We'll run each idea past two groups of reviewers — one composed of internal scientists, and another of partners and advisers with a history of identifying creative solutions to difficult problems. We expect many of these

projects to fail, but we stand ready to put substantial funding behind those that succeed.

We will begin taking submissions on the Grand Challenges in Global Health Web site on March 31 for a first set of four ambitious challenges. We're seeking new ways to protect against infectious diseases, drugs and delivery systems that limit the emergence of resistance, new ways to prevent or cure HIV infection, and an understanding of the basis for latency in tuberculosis. We'll issue new challenges at least twice a year going forward. We hope to hear from researchers of every age, on every continent, and from disciplines that don't typically focus on global health or even biomedical research — for history has taught us that great ideas can come from anywhere.

Each year, 9.7 million children die before 5 years of age, 4 million of them within the first month of life and the vast majority of them in the poorest countries in the world. These numbers are staggering to contemplate, let alone comprehend. Most of these deaths can be averted with the application of existing tools, but in some cases only new ideas will provide practical and effective solutions. Through initiatives like Grand Challenges Explorations, we hope to breathe life into the best of these new ideas.

Dr. Yamada reports holding equity in GlaxoSmithKline and Covidien. No other potential conflict of interest relevant to this article was reported.

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