A Global Road Map Is Needed For Vaccine Research, Development, And Deployment

Adel Mahmoud

Cite this article as:
Adel Mahmoud

A Global Road Map Is Needed For Vaccine Research, Development, And Deployment

Health Affairs, 30, no.6 (2011):1034-1041


The online version of this article, along with updated information and services, is available at:
http://content.healthaffairs.org/content/30/6/1034.full.html

For Reprints, Links & Permissions:
http://healthaffairs.org/1340_reprints.php

E-mail Alerts : http://content.healthaffairs.org/subscriptions/etoc.dtl
To Subscribe: http://content.healthaffairs.org/subscriptions/online.shtml

Health Affairs is published monthly by Project HOPE at 7500 Old Georgetown Road, Suite 600, Bethesda, MD 20814-6133. Copyright © 2011 by Project HOPE - The People-to-People Health Foundation. As provided by United States copyright law (Title 17, U.S. Code), no part of Health Affairs may be reproduced, displayed, or transmitted in any form or by any means, electronic or mechanical, including photocopying or by information storage or retrieval systems, without prior written permission from the Publisher. All rights reserved.
By Adel Mahmoud

ANALYSIS & COMMENTARY

A Global Road Map Is Needed For Vaccine Research, Development, And Deployment

ABSTRACT The world is witnessing a tremendous interest in the discovery, development, and use of vaccines as an important contributor to disease prevention and control. However, current global vaccine efforts are not coordinated, and they face many challenges. One is scientific: Most vaccines in use today are based on the scientific knowledge of past centuries. To usher in a new era, there is an urgent need to draw upon new science and scientific disciplines and recruit a new generation of talent trained in the basic and computational sciences of the twenty-first century. In addition, a global road map is urgently needed for making the scientific discoveries necessary to produce new vaccines; developing these into effective vaccines; and drawing up priorities and undertaking the necessary planning for rolling out these vaccines in developing countries. The developing countries themselves must play the lead role in these activities and contribute their own resources as well. This article aims to initiate a wide-ranging debate and discussion that will ultimately result in some agreement on the future of vaccine development and deployment.

At the turn of the current century, there was a renewed surge of interest in vaccines—this one of global dimension. The discovery and development of several new vaccines were both a catalyst and a result of this interest. New vaccines included the pneumococcal and meningococcal conjugates—vaccines in which antigens are chemically bonded with proteins to make the immune responses more effective in young children. Also in this group were vaccines that targeted rotavirus, the major viral cause of childhood diarrhea; human papillomavirus, which protects against cervical as well as anogenital and head and neck cancers; cholera; shingles; and several pediatric combination products. The twenty-first century also ushered in an era of pandemic influenza with H5N1 and H1N1, and concomitant efforts to develop vaccines for both.

The remarkable development of new vaccines and the rise of new epidemic threats coincided with the birth of the GAVI Alliance, originally called Global Alliance for Vaccines and Immunization. The organization, a public-private global health partnership founded in 2000, focused its efforts on vaccine use in the least developed countries. Since then, the GAVI Alliance has achieved a number of early successes—notably, the adoption of global hepatitis B vaccination. The growth of the global market for vaccines also led to the rapid advent of new vaccine manufacturers and expansion of existing manufacturers located in middle-income countries, which in turn resulted in the significant enlargement of worldwide vaccine manufacturing capacity.

In recent years, multiple innovative financing mechanisms for global immunization efforts also have been introduced, including the...
International Financial Facility for Immunization and the advance market commitment. These new initiatives, started by governments and philanthropic organizations, highlight how valuable vaccines are in the prevention and control of infectious diseases. Adding to the vaccine momentum, the 2010 United Nations Summit and the Bill & Melinda Gates Foundation launched the “Decade of Vaccines” initiative to spur progress in this field.

In spite of these exciting developments and the renewed focus on vaccines and global immunization efforts, there are reasons to reflect critically on the status of the whole effort. The number and variety of discovery and development efforts means that they often compete with each other for visibility and funding. In addition, there is no real global strategy for the broad introduction of new or recently developed vaccines for rotavirus or human papillomavirus. The multiple forces that shape the global vaccine map, such as international organizations, public-private partnerships, and advocacy groups, are not united in a vision. Nor are they in agreement about what steps to take to prioritize which vaccines will be rolled out in the developing world or which vaccines are urgently needed. Establishing such a priority list would help focus discovery and development efforts.

Additionally, the multiple agendas among the many vaccine players create tension. Disagreements are occurring among multiple scientific, policy, and advocacy voices on many fronts, such as which new vaccines need to be discovered or developed. The World Health Organization’s Initiative for Vaccine Research, Report 2008–2009 demonstrated the complexity and multiplicity of vaccine targets. Although the document served as a repository of all vaccine activities, it also provided ample evidence of the struggles that are under way to sort out which vaccine targets and directions to pursue.

Debates and differences of opinion are healthy if the outcome is a clearer vision. This article analyzes the fundamental aspects of global vaccine discovery and development that will determine the shape and outcome of the totality of efforts for decades to come. My aim is to initiate a wide-ranging debate that will galvanize and possibly add a degree of concordance to conflicting views about the future of vaccine development and deployment.

### Scientific Basis For Vaccine Discovery

The scientific basis of discovery of most vaccines currently available for human use is predicated on clinical or laboratory findings dating back more than two centuries. The often-repeated statement that vaccine discovery and development are based on both empiricism and art, rather than on clear theoretical or scientific advances made since this earlier era, is reflected in Exhibit 1.

#### Animal Pathogen

For example, the first principle for vaccine development was the use of an animal pathogen (cowpox) to immunize humans against smallpox and was introduced by Edward Jenner in 1796—more than a century before the discovery of viruses. This is the same technology that was used in the early 1900s to develop the widely used vaccine against tuberculosis, bacille Calmette-Guérin (BCG), and more recently in the production of the rotavirus vaccine, which is based on a bovine rotavirus platform.

This technology uses the characteristic exchange of genetic materials between human and bovine viruses, allowing the bovine virus to function as a carrier for the genetic materials of the human organisms, thus inducing protection.

### Exhibit 1

<table>
<thead>
<tr>
<th>Fundamental concept</th>
<th>Disease</th>
<th>Immunogen</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Animal microbes</td>
<td>Smallpox</td>
<td>Cowpox</td>
<td>1796</td>
</tr>
<tr>
<td>Attenuation</td>
<td>Rabies</td>
<td>Infected tissue</td>
<td>1881</td>
</tr>
<tr>
<td>Killed microbes</td>
<td>Cholera</td>
<td>Killed bacteria</td>
<td>1886</td>
</tr>
<tr>
<td>Toxoids</td>
<td>Tetanus</td>
<td>Heat treated</td>
<td>1890</td>
</tr>
<tr>
<td>Conjugation</td>
<td>Pneumonia</td>
<td>Capsular polysaccharide</td>
<td>1929</td>
</tr>
<tr>
<td>Virus propagation in cell culture</td>
<td>Poliomyelitis</td>
<td>Viral culture in cells</td>
<td>1949</td>
</tr>
<tr>
<td>Cloning of defined proteins</td>
<td>Hepatitis B</td>
<td>Surface antigen</td>
<td>1982</td>
</tr>
</tbody>
</table>

**Sources**

**LIVE AND KILLED MICROBES** The second principle for vaccine development, attenuation of live microbes, was first observed by sheer accident by Louis Pasteur in 1860, who then used the principle to develop vaccines against human rabies and anthrax. This approach—in which a live virus is weakened or attenuated so that it is no longer capable of making a person ill but can still stimulate a protective immune response—was also used nearly a century and a half later to develop one of the newly available rotavirus vaccines.

Around the turn of the twentieth century, two new principles for vaccine development were introduced. In one, the causative microbes of disease are killed. In the other, their toxins are modified in order to induce immunity without causing harm.

**CONJUGATES** Yet another principle of vaccine development was discovered in 1929 (Exhibit 1). However, the technology of conjugation—the chemical joining of complex sugars that make up the outer cell walls of bacteria to a protein backbone—has only been used in vaccines during the last two decades. Vaccines produced this way include one for *Haemophilus influenzae* type b (Hib) in 1997, for pneumococcus in 2000, and for meningococcus in 2001.

**PROPAGATED VIRUSES** In 1949 scientists discovered how to propagate viruses in cell culture. This advance made it possible to develop several vaccines for most childhood viral infections, such as poliomyelitis, measles, mumps, rubella, and varicella (chicken pox).

**RECOMBINANT TECHNOLOGY** We do not intend to minimize the tremendous achievements of the vaccine community over the past decades, but it is sobering to realize that with the exception of two relatively recent vaccines for human use—hepatitis B and human papillomavirus—most other vaccines are based on scientific empiricism and discoveries of past centuries.

Both the hepatitis B and human papillomavirus vaccines were discovered and developed in the last two decades of the twentieth century. Both are produced by recombinant technology, where a defined component of the virus is cloned in yeast or other systems for production of viral protein in vitro (meaning in an artificial environment outside of the living being). The scientific rationale for cloning these specific viral proteins was unclear at the start and remains poorly understood now. The cloned proteins of both viruses have to undergo a process of folding (internal molecular structural rearrangements) that results in what are known as virus-like particles. These are self-assembled structures similar to the whole virus but are made of only one protein component and devoid of all of the other genetic materials that constitute the complete virus.

The basis for this phenomenon of self-assembly is unknown, as is why these proteins produce protection in the host when they are folded correctly. As a matter of fact, these individual viral proteins, if used prior to appropriate folding, produce no protection in animal experiments and induce poor immune responses. A realistic assessment of the basis for this realization is that it was pure serendipity—a comment that should not detract from this remarkable discovery. Multiple attempts to isolate single protective molecules from many other microbial pathogens to evaluate their ability as vaccine candidates have uniformly failed to date, in spite of tremendously innovative new molecular and immunological tools.

**ADJUVANTS FOR HUMAN USE** One more recent and significant advance relates to the approval of two new so-called adjuvants for human use. Adjuvants are substances added to vaccines to increase their immune-producing effect. After decades of using alum salts as the only approved adjuvant for human vaccines, the approval of two new adjuvants, labeled AS04 and MF-59, paves the way to explore more specific and potentially more effective adjuvant molecules, which are urgently needed for new vaccine discovery.

**OTHER NEW VACCINE PURSUITS** The past two decades also witnessed a remarkable effort to discover and develop new vaccines, particularly against the three big infectious diseases (tuberculosis, malaria, and HIV) as well as several emerging infections such as dengue. Most of these efforts have yet to result in vaccines available for human use. In spite of the tremendous scientific discoveries of monoclonal antibodies, DNA sequencing, genomics, and detailed dissection of host immune responses, multiple hurdles still exist. The difficulties are both scientific in nature and in planning strategies for the future.

**Global Efforts For Vaccine Deployment**

The second aspect of this analysis of global immunization efforts concerns the way in which international entities are organizing themselves and others to advance the discovery and deployment of vaccines. The beginning of this century marked the birth of the GAVI Alliance to expand the reach of vaccines, particularly in the least developed countries, and to address the obvious delays in introducing new vaccines such as hepatitis B and Hib. Both vaccines were introduced in the developed world fifteen to twenty years before being deployed in developing countries.
Formation of the GAVI Alliance represented a major step forward in establishing a fresh set of approaches for developing and deploying vaccines. Forming the GAVI Alliance was not the choice of the global vaccine establishment; rather, it was an expression by new forces of the desire for major change. The leading roles of the Bill & Melinda Gates Foundation, the governments of several developed countries, the pharmaceutical industry, and academics were evident at GAVI’s inauguration—not only in securing initial funding but also in the insistence that all of these stakeholders should have seats on the board of the organization. The GAVI Alliance board includes representatives of governments and vaccine manufacturers from developed and developing countries; the main international organizations involved in health policies (such as the World Health Organization, UNICEF, and the World Bank); and representatives of philanthropic and civil society organizations, as well as several research institutions.

**PHASE I:** Phase I of the GAVI Alliance (2000–05) was marked by a disciplined focus on the introduction of new vaccines and enhanced basic immunization practices such as safe injections and disposal of used syringes. An example of the success of Phase I was the expansion of hepatitis B vaccine to a considerable percentage of children in the least developed countries. This expansion represented a landmark in global vaccination efforts. In 2000 hepatitis B vaccine was barely used in the seventy-two low-income countries targeted by the GAVI Alliance. At the conclusion of GAVI’s Phase I effort, the vaccine was administered to approximately 50 percent of the birth cohort in these countries. As a result of this success, financial support for the GAVI Alliance tripled for the organization’s next phase.

**PHASE II:** The goal of Phase II (2006–15) is reducing mortality for children under age five, which reflects one of the key United Nations Millennium Development Goals (goal 4). These goals were articulated by the United Nations at the beginning of the twenty-first century to galvanize a major push for reducing global poverty. The specific objective of goal 4 is to reduce the mortality rate by two-thirds among children under age five between 1990 and 2015. Achievement of that goal is fundamentally dependent on the global expansion of immunizations.

To implement such a goal, the GAVI Alliance determined it will make advanced vaccine products available to the world’s poorest countries and strengthen delivery systems to ensure that children in these countries derive the full benefits of immunizations. Although these are important objectives, GAVI has yet to define them with any specificity: which countries, which diseases, which immunizations. Additionally, it has not declared what quantitative measures will be used to demonstrate progress. More troubling is the fact that Phase II does not give specific guidance or priorities to developing countries about which vaccines to introduce or how to phase in a sequence of vaccine introduction programs.

**ROLE OF MIDDLE-INCOME COUNTRIES** In the meantime, there have been several important, but separate, developments in the global vaccine sphere as a result of the GAVI Alliance. Among the most important is the enhanced role of middle-income countries—such as India—as vaccine manufacturers. These manufacturers currently produce approximately half of the vaccines procured by UNICEF for the GAVI Alliance. Furthermore, this group of manufacturers is providing a basis for new vaccine formulations such as combination products that contain multiple vaccines (for example, for diphtheria, tetanus, pertussis, Hib, and hepatitis B), which used to be the sole domain of manufacturers in industrialized countries.

It is hoped that in the near future, vaccine manufacturers in middle-income countries will become involved in the development of new, effective vaccines such as the recently introduced cholera vaccine, manufactured by Shantha Biotechnics, part of the Sanofi-Aventis Group, and the meningitis A vaccine, manufactured by the Serum Institute of India. The continued expansion of vaccine manufacturers in middle-income countries is crucial to meet the urgent need for vaccines in many parts of the developing world.

**TWO IMPORTANT DOCUMENTS** The global vaccine expansion movement also triggered the publication of two important documents during the first decade of the twenty-first century. In 2005 the leadership of the World Health Organization and UNICEF approved the Global Immunization Vision and Strategy 2006–2015. This document focused on four general areas: immunizing more people; introducing new vaccines; making vaccination a component of health interventions; and positioning vaccines globally. The document provided useful information and guidance for the global community but lacked implementation strategies and financial backing.

In 2008 the two international organizations estimated the cost of maintaining global immunization at the 2005 level through 2015 to be $19.3 billion. If expansion were attempted, they estimated, an additional $16.2 billion would be necessary. These are lofty goals, and it remains unclear how such a plan may be funded.

In September 2010 the United Nations summit on the Millennium Development Goals published a document committing world leaders...
to a set of activities and goals to be accomplished by 2015 that included raising $40 billion for advancing women’s and children’s health. That commitment included an emphasis on sustaining and expanding prevention and vaccination programs.27

The overlap among these documents, organizations, and plans for global immunization, along with the call for a Decade of Vaccines, is considerable. The estimated costs of these efforts are tremendous, and yet there are no clear financing mechanisms. The many voices advocating for immunization, whether disease-specific or not, complicate plans for all other goals for economic and social development. It is no wonder, therefore, that a considerable degree of confusion is occurring between what developing countries perceive as their priorities and what international organizations, multiple public-private partnerships, and advocacy groups are calling for. The confusion and the multiplicity of players and agendas call out for a road map that all parties can embrace and use as a coordinating mechanism.

The Missing Elements

The challenge ahead is to define how decisions are made about global deployment of vaccines and their introduction into any specific country. In developed countries, such as the United States, first new vaccines are licensed by a regulatory agency, and then recommendations for use are delegated to advisory bodies.28 In most circumstances, the regulatory and advisory steps are followed by concurrence of professional and health care organizations. Financing may be secured either by governmental agencies or through health insurance coverage.

In contrast, in most developing countries there is no such established pathway for developing and introducing vaccines. Most developing countries either rely on the World Health Organization to approve a vaccine for global use, or they rely on the recommendations of that organization’s Strategic Advisory Group of Experts on Immunization. These recommendations are not country-specific. From that step, there is no clear pathway for vaccine assessment or how to plan introductions into an individual country.

Multiple reasons for these deficits, at either the national or the global level, may include inability to assess the burden of specific diseases, inability to prioritize, financial difficulties, and absence of political will. Other major deficiencies include weak infrastructures of individual countries’ health systems, particularly in connection with vaccine procurement, transportation, cold-chain maintenance to preserve vaccines whose temperatures must be controlled, and general administration. Under these circumstances, it is a challenge for a developing country to prioritize specific vaccination programs.

Given the inability of most developing countries to prioritize which vaccines to introduce nationwide, the decision-making process is left to what the international community proposes and what financial support mechanisms become available. But the multiplicity of special interests, lobbyists, and advocates leads to confusion and offers very little help to the leaders of most developing countries who are seeking advice and information. This puts the national leadership of developing countries in an awkward position, given the complexity of the global agenda for vaccines, mainly driven by donors, and their own perception of priorities and what they perceive as important for their own country.

Although representatives of developing countries are present in most of the global vaccine meetings and summits, the impact of the deliberations on domestic policies, priorities, and practices of these countries is unclear. Indeed, it is a tremendous challenge for these leaders to make vaccines and immunization a priority.

Global health is the concern of all national and global leaders and not simply the result of calls from outside the borders of developing countries. For example, how does a country rank-order vaccination programs amid other major global efforts to address malaria, HIV/AIDS, tuberculosis, and noncommunicable diseases? The future is directly linked to the health of children and adults in every country. If developing countries are unequipped to define and prioritize vaccination and immunization program needs, progress will be limited.

It is time to alter the debates about global health in general and vaccination specifically, and move them beyond the domain of intellectuals, scientists, and policy makers in the developed world and of international organizations. World leaders have to stop behaving like the American character in V.S. Naipaul’s novel A Bend in the River, who describes Africa as though the continent were a sick child and he were the parent.29 The decision-making process must be placed in the hands of those in charge in individual countries, with the expertise about the national priorities of developing countries to come from their national leaders.

In most of the global discourse about immunization, leaders of the developing world either stand by or simply agree on plans devised by others. If these developing countries are not able to articulate a set of clear priorities for the health of their own people, and to demonstrate leader-
ship and willingness to implement the necessary programs, the struggle against poverty, ill health, and lack of development will not go nearly far enough.

The myth that global immunization programs have to be funded by donors, international organizations, and philanthropies has to come to an end. This is not callous or cruel; it is simply a plea for leaders of the developing world and their populations to shoulder the responsibility of shaping their own future. National leaders have to show commitment and the ability to use their own resources, although small, in initiating and sustaining immunization efforts before they seek global support.

There are several examples of such countries, including Ghana and Vietnam. Rates of vaccination in both countries are remarkably high, and sizable national resources are used to partially fund these efforts. These countries have achieved successes in vaccination because of their own commitment of energy and money, not simply because some international donors handed them the cash.

Country-level leadership with a vision, determination, and persuasion is urgently needed for the global vaccine effort. There is no more room for paternalism. Maybe what is needed is reform: As Dambisa Moyo put it, the chief weapon in the “war on poverty” should be not aid but policy reform. This means that we need a concerted effort that involves leaders of developing and the developed countries as well as leaders of international organizations to agree on a road map moving forward.

What Is To Be Done?
The global science and health communities also have an opportunity to propel the vaccine effort forward, but we are at a crossroads. With the increased global interest in immunization manifested by the call for a Decade of Vaccines; the June 2011 Pacific Health Summit, which is to be devoted to vaccines; this issue of Health Affairs; and many other initiatives, a far-reaching debate has begun. The debate should result in a road map for global immunization efforts that includes the following objectives.

Focus on New Sciences First, there is no alternative for the future of discovery and development of new vaccines and improving some of the currently available products than a determined focus on basic understanding of microbes, their genes, and products. What is needed is not more of what we, the global scientific community, feel is in our comfort zone. New sciences such as genomics, structural biology, and computational understanding are reshaping our fundamental knowledge of microbes. We urgently need a new generation of specialists from developed and developing countries who are comfortable and experienced in these new sciences.

Specific Goals and Objectives Second, we need to develop focused and quantitative measures for what we plan to implement and what outcomes are to be achieved. The global community is tired of sloganeering and lofty unrealized goals. There must be concrete objectives for whatever programs are designed, and measures are needed that can be evaluated at reasonable intervals, measures such as vaccination rate for a specific vaccine, the rate of introduction of new vaccines, and use of new vaccine technologies.

National Leadership Third, national leaders must shoulder the responsibilities for using their resources in ways that benefit their country. They must provide evidence to their people and the global community that they are committed to the health of future generations.

Global Activism Last, we need global activism and champions who stand up for what is right and do not hide behind politically convenient slogans.

Conclusion
This assessment of the scientific basis for vaccine discovery and development, and the extent of our achievements to date, brings the global community to a fork in the road. Repeated attempts to discover new vaccines are being pursued in vain. Instead of continuing efforts based on dated scientific methodologies, it is imperative to develop new pathways in discovery of urgently needed vaccines.

In spite of the successes of the past two decades in developing several new vaccines, all of these were developed based on old principles. The recent history of vaccine development produces the inescapable conclusion that we need new ways of thinking and approaches. We need a new generation of scientific talents not beholden to futile attempts and methods.

These individuals should come from scientific disciplines such as genomics, metabolomics (metabolic changes induced in cells following infection), computational studies, and quantitative sciences—disciplines that traditionally have not been major players in vaccine discovery and development. These scientists will provide fresh eyes and possess capabilities that should address the challenge in new ways. They will be charged with following through on Joshua Lederberg’s adjuration—from his 2000 masterpiece on the history of infectious disease, titled “Infectious History”—that we must match “our wit against their genes” to combat microbial diseases.
This new generation will be charged with developing a more detailed and comprehensive understanding of microbes and defining the microbes’ most susceptible structures to the host’s immune response as the first step in the right direction. Our incomplete understanding of the forces of evolutionary biology results in a rush to use the host’s immune response as a lead to define potential vaccine targets. This is a simplistic assumption based on predicting that microbes will expose their most susceptible structures to the host’s immune-protective mechanisms. If that were true of the phenomenon of infection and parasitism, no infectious organism could have survived over the millennia and would have disappeared from nature many centuries back.

What is needed, therefore, is a return to basics, to examine and define microbial structures, organization, genomics, and metabolomics in an attempt to characterize their significant and crucial elements of survival in a host. Only then will the induction of protective immune responses—responses against specific susceptible components of the microbe—pave the way for the discovery and development of a new generation of vaccines.

The time is now to initiate a global effort aimed at exploring infectious diseases based on new scientific principles. The effort should be multidisciplinary and global in nature, involving new generations of scientists from developing and developed countries.

The author dedicates this article to the memory of Health Affairs Deputy Editor Phil Musgrove.

NOTES
13 Jadhav S, Datla M, Kreeftenberg H, Hendriks J. The Developing Countries Vaccine Manufacturers’ Network (DCVMN) is a critical constituency to ensure access to vaccines in developing countries. Vaccine. 2008;26(13):1611–5.
25 World Health Organization. Global immunization vision and strategy


Moyo D. Dead aid: why aid is not working and how there is another way for Africa. 1st ed. Toronto: Douglas and McIntyre Ltd.; 2010.


ABOUT THE AUTHOR: ADEL MAHMOUD

Adel Mahmoud is a professor at Princeton University.

In this issue of Health Affairs, Adel Mahmoud of Princeton University calls for formulating a global road map for vaccine discovery, development, and deployment. Mahmoud joined the Woodrow Wilson School of Public and International Affairs and the Department of Molecular Biology at Princeton after retiring in 2006 as president of Merck Vaccines and as a member of the management committee of Merck and Co.

Mahmoud’s experience at Merck clearly informs his call for new science. He led the development of four vaccines at the company: a combination vaccine for measles, mumps, rubella, and varicella (chicken pox); a rotavirus vaccine; a vaccine for shingles; and the vaccine for human papillomavirus. “Vaccine discovery and development is not only a scientific challenge, but a very complex set of decisions that tax many of our decision-making capabilities,” he observes. Hence his call not just for a new generation of scientists who will explore the frontiers of genetics and microbiology, but also for those with advanced expertise in computational science.

Mahmoud was born in Cairo and got his medical degree from the University of Cairo and a doctorate in clinical tropical medicine from the University of London, School of Hygiene and Tropical Medicine. Before his time at Merck, Mahmoud spent twenty-five years at Case Western Reserve University and the University Hospitals of Cleveland, including as chairman of medicine and physician-in-chief. His academic pursuits focused on determinants of infection and disease.

Mahmoud is a fellow of the American College of Physicians and a member of the Institute of Medicine, National Academies. He is the author or editor of several textbooks, reports, and many scientific publications.

At Princeton, Mahmoud’s current research interests are the global burden of infectious diseases and efforts for prevention and control. In particular, he is focused on introduction of rotavirus and human papillomavirus vaccines in the developing world.