

Vaccines: Science, health, longevity, and wealth

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Vaccination is considered the most successful and cost-effective medical intervention ever introduced (1). A recent publication from the US Centers for Disease Control and Prevention suggests that this distinction continues to hold, reporting that for children born in the United States during the period 1994–2013 vaccines will have prevented 322 million illnesses, 21 million hospitalizations, and 732,000 premature deaths, saving \$295 billion in direct medical costs and \$1.38 trillion in total societal costs (2). In a period of technological revolution and limited resources, we may think that our society would prioritize investing in the field of vaccine development insofar as it simultaneously protects health and saves money. Unfortunately, this is not the case and the future of vaccines is in jeopardy.

The special issue of the centenary of PNAS provides an opportunity to review the history of vaccines, the most exciting features of vaccine science, and to contemplate the future. The picture that emerges is intriguing: The history of vaccines confirms that vaccines have been the medical intervention with the greatest beneficial impact on human health and longevity (3). Vaccines dramatically reduced the incidence of infectious diseases that historically killed hundreds of millions, and made a substantial contribution to life expectancy that during the last century in developed countries increased from ~47–80 y (4). During the last 30 y, improvements in our understanding of immunology and technological progress involving recombinant DNA, conjugation technology, and genomics provided vaccines against diseases, which could not be conquered by conventional vaccine technologies. Finally, new, emerging, more powerful technologies, including rationally designed adjuvants and systems biology (4–6), raise the possibility of new and better vaccines that may allow better control of existing diseases and extend the benefits of vaccination to newly emerging infectious diseases and to noncommunicable diseases as well.

In the next few decades vaccines have the potential to continue to be the most powerful

tool for advancing global health and contributing to human well-being by (i) extending the benefits of vaccination beyond childhood and especially among pregnant women and the elderly; (ii) providing tools to prevent and control emerging infections, such as pandemic influenza and HIV; (iii) preventing and controlling noncommunicable diseases, such as cancer, neurodegenerative, autoimmune, and metabolic disorders that are the leading causes of morbidity and mortality in modern society; (iv) extending the benefits of vaccination to low-income countries so that during the next two decades we can close the health and longevity gap between poor and rich countries (4, 7); and (v) controlling most of the existing, and reducing the emergence of, antibiotic-resistant bacteria (8).

The bitter truth is that although vaccines keep people healthy and save money, fewer and fewer pharmaceutical companies invest in the development of new vaccines. Rather, their investment dollars are channeled disproportionately to new drug therapies in areas such as oncology, immunology, inflammation, and cardiovascular, metabolic, and neurodegenerative diseases, for which the return on investment tends to be higher and more predictable than for vaccines. A large part of the problem lies with the cost-effectiveness models policymakers commonly use to value vaccines, which demonstrate the cost-effectiveness of modestly priced vaccines that prevent large numbers of cases of mild diseases, but not of

more costly vaccines that prevent rarer and often life-threatening diseases (9). The consequence is that industry, to maximize shareholder returns, prioritizes investments in therapies and deprioritizes investment in vaccines.

How did we end up in this situation, in which the allocation of resources for medical research is increasingly skewed against vaccines? The problem lies partly in the cost-effectiveness approach, which typically accounts for averted medical care costs and loss of parental work time to care for sick children, and not the full benefits of health to such items as lifetime income and wealth accumulation, and its economic spillover effects on the broader society. Several initiatives are trying to radically change the economic evaluation of vaccines; these are described in an article on valuing vaccination in this special issue (10), in the SMART Vaccines initiative of the Institute of Medicine that describes 28 attributes to be considered in vaccine prioritization (11), and in ref. 9. Understanding the value of vaccines to our society and taking this value properly into account in the allocation of resources to vaccine development are both essential to realizing the continuing contribution vaccines can make to human well-being and progress.

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