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Arthur L. Caplan
Jason L. Schwartz

Vaccines present a spectrum of unique ethical considerations compared with those associated with other medical interventions. Central to these differences are the role of vaccines in disease prevention rather than treatment, the concurrent interest of vaccination policy in improving the health of communities and individual people, and the focus on children in many vaccination programs. Formal discussions of ethical issues related to vaccination were once concentrated largely on aspects of clinical research and specific topics regarding vaccine safety and financing. Recent events, such as the arrival of vaccines against human papillomavirus (HPV) and the 2009-2010 H1N1 influenza pandemic, have demonstrated the need for a more comprehensive and proactive examination of vaccine ethics. Such an approach offers important insights into all aspects of the vaccine life cycle, from the earliest stages of research through deployment in national and global immunization programs.

Ethical issues unique to vaccination

Ethics of prevention vs ethics of treatment

Unlike pharmaceuticals and most other medical interventions, vaccines are intended to prevent disease rather than treat it. The ethics of prevention differ greatly from the ethics of treatment. Chief among these differences are the disparate meanings and interpretations of "risk" in each context.

When treating disease, risks are largely confined to two broad categories: the risks associated with a particular intervention and the risks of doing nothing. These risks are weighed against the potential benefits of a specific treatment and compared with the risk-benefit profiles of potential alternatives. Decision making is invariably complicated by the uncertainty associated with any assessment of risks and benefits. Nevertheless, a treatment decision is made based on the evaluation of all options in light of the risks and potential benefits of each, all compared with the consequences of doing nothing.

When aiming to prevent disease by means of vaccination, assessing the risk of inaction is more challenging. Here, the physiological consequences of a disease in an individual person must be considered *in addition to* the specific likelihood of acquiring that disease. As a result of successful vaccination programs, the incidence of many vaccine-preventable diseases is extremely low in the United States and other developed nations. This complicates efforts to convey the continued necessity of vaccines to parents, many of whom may have never seen or experienced the diseases being prevented. Globally, the risk of disease is subject to wide geographical, national, and occupational variability. In all cases, high rates of vaccination among communities are widely credited with preserving the low incidence of many vaccine-preventable diseases.[1]

The benefit of high vaccination rates highlights a key difference between the ethics of treatment and the ethics of prevention. Prevention, particularly the prevention of infectious diseases through vaccination, has important implications for individual people and communities. While considerations relative to justice and the allocation of scarce resources have ethical relevance to some treatment decisions, rarely are they primary factors in how care is delivered.

As a form of prevention, vaccination requires the juxtaposition of individual autonomy with societal best interests. These values are often in alignment, but for some persons, they present competing arguments regarding the decision to vaccinate. Central to this debate is herd immunity, the additional protection against a disease that is a result of high vaccination rates in a community. Some persons believe that the benefits of vaccination are outweighed by the associated risks, however small they may be. This is a particularly likely scenario for the diseases that have virtually disappeared in wealthy nations due in part to successful vaccination programs. The people choosing not to be vaccinated would still receive some protection because of herd immunity, creating the potential ethical problem of responding to "free riders".

Free riders are people who share in the benefits of vaccination programs without personally assuming any vaccine-related risks or costs, such as the risk of adverse events or the time and expense required to receive vaccinations. Recent vaccine-preventable disease outbreaks among unvaccinated persons suggest that personal reliance on herd immunity for disease protection is often inadequate.[2,3] Such decisions also increase the overall risk of disease in communities, particularly for the members too young to receive a vaccine or unable to do so because of medical contraindications.[4] People who knowingly benefit from the actions of others without sharing in the burden or cost of providing that benefit act in an unethical manner.

Target populations and the routinization of vaccines

The significance of healthy children as the largest target population for vaccines cannot be overstated. Young children are ethically vulnerable because they cannot exercise their own autonomy to mediate issues of risk and benefit. With a majority of vaccinations in the United States recommended for children in the first 24 months of life, vaccine recipients are typically among the most ethically vulnerable of populations. While striving to make decisions that are in a child's best interests, parents and guardians must navigate a sea of at times

conflicting information related not only to vaccines, but also to all aspects of a child's medical care.[5,6] The heated, heavily publicized debates about the safety and value of vaccinations in recent years have added to the challenges faced by parents aiming to make responsible and informed decisions about their children's health.

Ironically, communication efforts may be hampered as a result of how routine childhood vaccination has become in many parts of the world. Amid competing demands on health care providers, efforts to explain the continued importance of vaccination to parents may suffer. Absent unique concerns raised by parents or providers, communication about vaccines may be left instead to a few short questions and answers or reliance on government-required printed information statements.[6] The routinization of vaccines is amplified by state laws in the United States requiring vaccination against many diseases as a condition of school or day-care attendance. This atmosphere of familiarity partly explains the widespread alarm generated by reports of vaccine-related safety concerns, regardless of whether the concerns are confirmed or only alleged.

Ethical considerations in the vaccine life cycle: an overview

While the preceding discussion highlights some of the unique attributes of vaccines and vaccine decision making, their research, development, and regulation are similar in form and function to those of pharmaceuticals and other medical interventions. In the following sections, we provide an overview of relevant ethical considerations at various stages of the vaccine life cycle, a period that begins with the earliest basic research and extends through licensure and all dimensions of national and international vaccine production and distribution programs.

Research and development

Throughout the modern history of vaccines, the successful development of new discoveries has relied on collaborations between academic medicine and the pharmaceutical industry. More recent additions to these collaborations have been smaller biotechnology companies that typically conduct early vaccine development before licensing their successful products to larger manufacturers. While financial support for these activities has traditionally come from a combination of investment funds and government-sponsored research awards, philanthropic groups have become increasingly interested in vaccine development in recent years. Particularly for diseases more common in the developing world, these philanthropic entities often bring substantial financial resources to support their research interests.

Such a diverse group of research entities and funders all but assures a collection of differing research priorities, objectives, motives, and measures of success. While all contributors share the general aim of developing safe and effective vaccines, conflicts may arise regarding how best to achieve this goal. If unchecked, such conflicts could impede progress toward novel vaccines, waste limited financial resources, and fail to respect the contributions of human research subjects. Large research partnerships have the potential to advance public health in ways that would occur much more slowly, if at all, if attempted by individual entities. While respecting their obligations to shareholders, boards, or other overseers, all contributors to vaccine research and those who invest in their work should remain keenly aware of the morally distinguishing ability of their work to save lives, prevent suffering, and improve global health.

Research partnerships become even more ethically complex when including clinical research in developing nations. This is increasingly important as more vaccine development efforts target diseases common in the developing world, often through collaborations in which Western researchers have a leading role. These activities bring needed expertise and capabilities to nations often lacking robust medical research infrastructures. During this process, however, local researchers and health ministries ought to be involved in a meaningful way in all aspects of clinical research taking place in their country. The benefits of such relationships are many. For example, they may provide additional knowledge and training for local health officials, expertise that could benefit communities long after research has concluded. Meaningful contributions from local officials also create an additional layer of protection to ensure that the generosity of volunteers is not exploited by research that might have been deemed unethical had it been proposed for populations in developed nations.

No topic related to vaccine research has generated more controversy on ethical grounds than the designs of clinical trials, particularly those in the developing world.[7–11] As an example, one notable debate during the past 15 years has centered on HIV vaccine trials in the developing world, particularly the level and duration of care that ought to be provided to research subjects who become infected during trials.[12–17] Options range from lifelong treatment with the latest in antiretroviral medications—the norm in many developed countries but highly uncommon elsewhere—to whatever the typical treatment is in the country where the trial took place. Such a level of care is often well below that of the research sponsors' home countries. It may be nothing. Because of the significant consequences of this debate to the feasibility of future research, attempts at reaching consensus on the question of which standards should prevail have largely failed.[12,14] This long-standing and still unresolved debate provides a useful example of the value of robust discussions of ethical considerations *before* controversies develop and decisions cannot be undone.

Vaccine development can never be immune from the twin pressures of personal advancement and corporate profitability. Nevertheless, the world community is best served by vaccine research programs that match these concerns with a continued acknowledgment of the enormous suffering that can be averted by vaccines and respect for the individual people and communities volunteering to assist in clinical research.

Finally, concern for justice requires that the populations in which a vaccine candidate is studied mirror as closely as possible the groups expected to receive the licensed product. The use of mentally handicapped children as primary sources of vaccine research subjects in the 1950s and 1960s exemplifies how this principle was violated in the past.[18] The children often lived in overcrowded institutions with sanitary conditions that placed them at increased risk for the diseases for which potential vaccines were being tested. New vaccines would have been particularly valuable to the children, who also provided a convenient, accessible study population for researchers.

However, mentally handicapped children in state institutions are among the most vulnerable of populations, for whom clinical research is ethically appropriate only in extremely limited circumstances and always with strict oversight. In pursuit of vaccines that would benefit society broadly, the past use of these children as a primary study population often violated this fundamental tenet of research ethics.

Today, the opposite extreme has become common. Manufacturers have a strong disincentive to include among their research subjects members of potentially high-risk populations, such as pregnant women or children with intellectual disabilities. Without complete data on safety and efficacy in all populations to whom a vaccine will be administered, patients, parents, and policymaking bodies have inadequate information

on which to base their decisions regarding vaccination in these groups. The vaccine research and regulatory communities should remain cognizant of past exploitation of vulnerable research subjects but strive to conduct clinical research in ways that protect subjects while providing as complete a picture as possible of a vaccine's safety and efficacy profile.

Licensure and safety monitoring

Vaccines are subject to oversight and regulation by a variety of entities in every country where they are available.[19] It is initially determined whether a new vaccine should be licensed, and if so, the populations for whom it should be recommended. In the United States, these responsibilities belong to groups within the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC), respectively. For the life of the vaccine thereafter, activities are undertaken by these groups in collaboration with its manufacturer to monitor its safety and efficacy.[20] These processes have generated considerable controversy in recent years, threatening to damage public confidence in vaccination.[21] Since the success of vaccination programs depends on earning and maintaining public trust, there are several points in vaccine regulation at which ethical considerations are relevant to public policy.[8,22]

A primary concern of critics of vaccine policy in the United States is the potential for conflicts of interest among government advisors and researchers who have ties, financial or otherwise, to vaccine manufacturers. The very nature of vaccine development presents unique challenges in avoiding even the appearance of a conflict. Any researcher working on novel vaccine candidates *must* eventually partner at some point with industry owing to the infrastructure needed for large-scale clinical testing and development. To exclude all such researchers for this reason would be to forfeit a wealth of expertise and wisdom on vaccine science and policy, ignoring internationally respected leaders in vaccine science.

However, the importance to vaccination programs of maintaining public trust demands that those contributing to policy exercise particular caution and care regarding their professional and financial relationships. Most advisory bodies have clear policies regarding the disclosure of potential conflicts of interest.[23] Even when confident that financial relationships would have no impact on their actions, individuals should remain particularly attentive to how such interests might affect the manner in which the decisions to which they contribute may be perceived. Transparency, minimization of personal gain, divestiture, and disclosure are crucial principles that work to counteract the perception of conflict of interest influencing decision making.

Public attention to conflicts of interest among policymakers and their expert advisors is often linked to reports of vaccine safety concerns. The public health and regulatory communities should respond vigorously to reports of vaccine-associated adverse events, even if they initially seem unlikely. Passive surveillance programs such as the Vaccine Adverse Event Reporting System in the United States are valuable tools in this effort, but their limitations as hypothesis-generating mechanisms should be clearly conveyed to the public and the media.[24] Emerging patterns of possible safety problems should be explored thoroughly, with the results of these analyses promptly communicated to the public. Even when evidence suggests that a reported safety concern is unfounded, experience has shown it is unlikely that any such assurance will allay the worries of all. Open, expeditious, and detailed examinations of possible vaccine-associated safety concerns are nevertheless essential to maintaining overall confidence in vaccination programs and their oversight.[21,25]

It is inevitable that a small number of persons will genuinely be harmed as a result of vaccines. Since vaccination benefits communities, victims are entitled to compensation for their suffering in these rare cases. In the United States, the Vaccine Injury Compensation Program is the principal mechanism for resolving such issues.[26] By means of a no-fault system with funds collected via a tax on every vaccine dose, the system provides compensation without exposing manufacturers to substantial financial risk.

This program has faced scrutiny in recent years regarding how claims are resolved and the scope of its coverage. The Omnibus Autism Proceeding and the case of *Bruesewitz v Wyeth* heard by the US Supreme Court in 2010 represented challenges to aspects of the federal government's system for identifying and compensating for vaccine-related injuries.[27,28] Given the concomitant challenges of compensating victims fairly, accurately distinguishing correlation from causation regarding adverse events, and ensuring that manufacturers remain committed to developing and manufacturing vaccines, the current design of the Vaccine Injury Compensation Program is a generally fair way of resolving these ethical obligations.

Vaccine supply, access, and financing

The highly publicized influenza vaccine shortage in 2004 and many other shortages for recommended childhood vaccines underscore the vulnerability of vaccine supply worldwide.[29] With limited manufacturers and often only a single licensed product available in a country, vaccines are highly susceptible to large fluctuations in supply and availability owing to unforeseen events.[30–32] In the United States, CDC stockpiles of recommended vaccines are maintained to provide a temporary buffer in case of production or supply problems, but these efforts provide only limited protection.[33,34]

A spectrum of economic and business considerations help explain why manufacturers have left the vaccine market and why the remaining manufacturers are not eager to develop new products to compete with older vaccines that, in general, are able to meet demand.[30,31] Increasing the number of vaccine manufacturers and developing new vaccines for common diseases would help to ensure a more resilient vaccine supply landscape better insulated against the shortages that have become increasingly common.

Even when vaccine supplies are adequate, vaccination rates reflect many of the same racial and ethnic disparities in access present throughout medicine.[35,36] While the underlying causes of these conditions are debated, several programs seek to eliminate vaccine cost as an obstacle to childhood vaccination in the United States, most notably the Vaccines for Children and Section 317 grant programs for uninsured and underinsured children.[37] These programs make vital contributions to childhood vaccination rates, but aspects of their administration generate ethical dilemmas for state health departments and health care providers.

The introduction of newly licensed and recommended vaccines, often with far higher prices than older products, has outpaced the growth of Section 317 funds available for vaccination programs in many states.[38] This has forced state health officials to decide which CDC-recommended vaccines to make available to children when unable to afford them all. If required to ration state public health funds available for public-sector vaccine purchase, state policymakers should make decisions informed by the best available data, state-specific epidemiology, and comparative cost-effectiveness of each option under consideration. At the same time, advocates for vaccination have an obligation to raise awareness of inequities in vaccine financing and access.

Private health insurance plans generally provide coverage for CDC-recommended vaccines for children and adults, but they may require substantial patient copayments for some vaccines or fail to reimburse health care providers fully for related administrative costs. As a result, financial barriers remain for many patients and providers even when private insurance is available.

According to the Institute of Medicine, an estimated 11 million children and 59 million adults have private insurance that does not adequately cover costs related to immunization.[39]

As part of the 2010 Affordable Care Act, new insurance plans must provide coverage for any vaccine recommended for routine use in children or adults by the CDC Advisory Committee on Immunization Practices (ACIP).[40] No copayment, coinsurance, or deductible can be required from the insured patient. This provision for vaccines is part of a spectrum of preventive services required of new private insurance plans. Over time, these requirements are likely to bring transformative benefits to efforts already underway to promote prevention. How this legislation will ultimately reshape existing programs for promoting and financing childhood vaccination remains uncertain.

In comparison with children and insured adults, uninsured adults face far greater financial obstacles to vaccination. With an increasing number of vaccines recommended for adults but no program similar to Vaccines for Children, vaccine affordability for uninsured adults is likely to become a growing concern despite ongoing attempts at health insurance reform. Already, there is evidence suggesting the detrimental effect of vaccine cost concerns on uptake of herpes zoster (shingles) vaccine for adults 60 years or older and HPV vaccine for young adults older than 18 years.[41] Federal and state governments, in collaboration with vaccine manufacturers, should identify strategies that reduce these financial obstacles to adult vaccination. The laudable patient assistance programs recently introduced by several vaccine manufacturers may provide a foundation for more expansive efforts in this area.

Vaccination mandates

Governments worldwide use a variety of approaches to promote high vaccination rates among their citizens.[37,42,43] The United States is generally unique in its reliance on federal recommendations coupled with state school-entry vaccination requirements as central to the success of vaccination efforts. While specific requirements vary among states, all mandate that children receive a series of vaccinations as a condition of attending public school or state-licensed day-care facilities.[44] Every state allows for exemptions based on medical grounds, and nearly all also accept religious or philosophical reasons, although not every state includes all three types of exemptions.[45]

No topic related to vaccine ethics in the United States is more frequently debated than state vaccination mandates. The debate reflects a common tension in public health policy between individual (or parental) autonomy and the public good. Vaccines are mandated not primarily to protect the health of any particular individual, but to ensure that the transmission of diseases through communities is limited to the greatest extent possible. School-entry requirements are seen by public health officials as essential to maintaining vaccination rates sufficiently high to preserve herd immunity.[46] This provides additional protection against vaccine-preventable diseases to all members of a community, including those too young to receive vaccines or unable to do so because of medical contraindications.

For persons whose views on medical ethics are guided by the primacy of patient autonomy, it is understandable why US vaccination mandates are so contentious. However, few contemporary ethical models place autonomy absolutely above all other considerations. Instead, respect for autonomy is typically one of several factors that should be examined in light of other relevant considerations as part of ethical deliberation and decision making. There is a compelling argument that the lives saved and suffering prevented by vaccination outweigh the potential infringement on personal autonomy created by school mandates. While one may be free to make medical decisions that place his or her own health at risk, he or she may not jeopardize the health of others, a consequence of low vaccination rates within a community. Even in an autonomy-oriented culture such as the United States, there are ethical reasons to place some limits on individual choice.

An ethically preferable scenario would be maintaining current high rates of vaccination without needing the force of mandates to do so. Absent evidence that this is attainable in the United States, the current policy is sound. Mandates serve as a "safety net", a valuable tool to call attention to the importance of vaccines and help direct government and public health resources to vaccination efforts.[44] Exemption policies provide a ready alternative in nearly all states for persons whose personal beliefs do not coincide with protecting public health. Combined with incomplete enforcement by state health departments or local school districts, current policies fall far short of true compulsion. They are instead best understood as presumptive or default approaches to vaccination.

While national rates of nonmedical exemptions remain quite low, recent trends—particularly within select communities—are of deep concern to advocates of vaccination.[47] Overall, however, a large majority of Americans continue to believe in the value of vaccination for themselves and their children despite occasional controversies regarding the necessity or safety of vaccines.

Special topics in vaccine ethics

Human papillomavirus vaccines

Vaccines against HPV have raised a spectrum of ethical and policy considerations since their arrival in 2006. Initially, some critics expressed concern that HPV vaccination might negatively influence decisions made by teenagers about sexual behavior, increase the likelihood of promiscuity, and provide a false sense of security as to protection against sexually transmitted infections.[48] Evidence suggests that HPV is a very small factor in decisions about sexual behavior among teenagers, however.[49] Since at least 30% of cervical cancers are caused by HPV strains not included in current vaccines, education remains essential to convey the importance of continued vigilance regarding cervical cancer screening as part of comprehensive prevention programs.

Shortly after the licensure of the first HPV vaccine in the United States in 2006, many states introduced legislation that would add the vaccine to those required for school attendance.[50] An executive order by Texas Governor Rick Perry in early 2007 that mandated the vaccine for sixth-grade girls generated considerable controversy nationwide.[50] The executive order was overturned by the Texas legislature, and, as of early 2012, only Virginia and the District of Columbia have adopted HPV vaccine requirements. However, extremely liberal exemption clauses mean that these "mandates" are little more than "opt-out" policies.[51]

There is broad agreement that vaccine requirements should be considered only after a new vaccine is well established. This includes stable financing and supply arrangements, evidence of long-term safety, and successful educational initiatives for parents and health care providers.[52] While well intentioned, early efforts to mandate HPV vaccination were premature, and the negative attention they generated may have been a distraction to overall HPV vaccine educational efforts.

The approval of two similar but distinct HPV vaccines in the United States and many other countries presents additional ethical challenges with respect to the prevention of genital warts.[53] While both vaccines provide comparable protection against two HPV strains responsible for a majority of cases of cervical cancer, the quadrivalent vaccine manufactured by Merck and Co. also includes protection against two additional strains of HPV that are the most common causes of genital

warts in both sexes. Genital warts are not fatal but require medical evaluation and treatment. Commentators have noted the significant emotional impact on quality of life owing to genital warts, a condition more common among adolescents and young adults.[54] Public and private sources of vaccine financing must carefully consider how to assess the benefits of both HPV vaccines and evaluate the importance of genital wart prevention relative to the far more publicized role of these vaccines in preventing cervical cancer.

Related ethical considerations are raised by the vaccination of males against HPV. In 2009, the quadrivalent vaccine was licensed by the FDA for use in males for the prevention of genital warts.[55] An expanded indication for the prevention of anal cancer in both sexes was added in 2010.[56] Potential indirect benefits of male HPV vaccination include the additional reduction in cervical cancer incidence that would result from targeting a reservoir for the virus. Economic modeling of male vaccination efforts was generally unfavorable in 2009-2010, suggesting that concentrated attention to improving vaccination coverage in females was the preferred strategy for HPV-related disease prevention. However, encouraging both sexes to receive the vaccine appeals to fairness and simplifies promotional efforts. It would also symbolize the shared responsibility of men and women in the prevention of cervical cancer and other sexually transmitted infections.[53]

The ACIP initially opted against a routine recommendation for male HPV vaccination, instead adopting in 2009 a "permissive use" statement that acknowledged that the vaccine was available for persons who want it. Based on new information about the effectiveness of the vaccine and additional economic modeling data, the panel revisited its guidance in 2011. Its amended recommendations now endorse routine use of the quadrivalent vaccine in males aged 11 or 12 years and in unvaccinated males up to 21 years old.[57]

Health care providers

Health care providers have a twofold role in the success of disease-prevention efforts through vaccination. Considerable evidence points to the importance of recommendations from physicians and other providers in influencing the decisions of parents regarding vaccines.[58] Amid conflicting information and contentious debates about the safety, effectiveness, and value of vaccines, health care providers can help patients (or more often parents or guardians) make decisions about vaccination based on the best available evidence. Doing so requires sustained attention by providers to new information about vaccines—particularly vaccine safety—and the time and willingness to engage parents with concerns or uncertainty. Some pediatricians have chosen to decline to care for patients whose parents decline to receive the CDC-recommended vaccination schedule. This approach is not endorsed by the American Academy of Pediatrics, and it raises the concern that not all of these parents will seek or find alternative care for their children.[59]

Health care providers can also demonstrate the value of vaccination by ensuring that they are personally up-to-date on recommended vaccines. Beyond the symbolic value of this action, vaccination of providers protects patients, particularly in hospital settings where diseases like influenza are easily transmitted.

Maintaining high vaccination rates against seasonal influenza among health care providers has proven to be a considerable challenge, despite the vaccine being recommended for this group since 1981.[60] A variety of programs, including those involving incentives for compliance and appeals to professional duty, have failed to yield adequate vaccination rates, prompting an increasing number of health care facilities to mandate annual influenza vaccination as a condition of employment.[61] In light of the consistent failure of voluntary approaches to improve influenza vaccination rates among health care workers, mandatory vaccination policies are an appropriate response, particularly in light of the increased susceptibility for infection among many patients in hospitals and related settings.[60]

Vaccination in the developing world

Special ethical considerations related to vaccines in the developing world extend beyond the research issues discussed previously. A particular challenge is ensuring that new vaccines are introduced against diseases that are most prevalent or most severe in those nations but uncommon or mild in developed countries. Owing to the limited profitability of such vaccines, manufacturers are often reluctant to invest in these efforts.[62,63] Much of this work is therefore supported by private philanthropies, nonprofit entities, and public-private partnerships. These efforts should continue to be encouraged so that the benefits of vaccination may be more equitably distributed among all populations. For vaccines developed by corporate manufacturers, work should continue to develop financing arrangements that deliver existing products to populations in the developing world that often would benefit most from them.

When organizing vaccine distribution programs, particular respect should be paid to cultural traditions and social customs specific to communities in the developing world. In locations where health care infrastructures are radically different from those of wealthy nations, successful vaccination efforts depend on embracing these differences, valuing the input of community leaders, and striving to develop programs that gain widespread support.

Finally, efforts should be undertaken to better understand the concept of consent in the context of developing world vaccination programs. Informed consent in the strict Western sense may not always be attainable, nor may it be a reasonable expectation owing to the varying structures of communities and families present throughout the world. However, vaccination efforts should remain faithful to the spirit of informed consent, with those administering vaccines taking steps to ensure that recipients receive much more from vaccination programs than the vaccine dose alone.

Eradication campaigns

The global eradication of smallpox, certified by the World Health Organization in 1980, remains one of the foremost triumphs in the history of public health.[64] By means of a coordinated, extensive vaccination campaign, a disease that had been the cause of untold suffering and death for centuries was effectively eliminated. The successful eradication of smallpox added to the enthusiasm for other eradication campaigns against vaccine-preventable diseases, including those already underway and others hypothesized at the time. This enthusiasm has continued, despite as yet insurmountable challenges in adding additional diseases to the list of those eradicated.

Measles and polio have long been among the most prominent targets of eradication efforts, and eradication is now mentioned as a target for malaria, a disease for which a partially effective vaccine recently has been developed.[65] In recent years, most attention has been directed toward the potential eradication of polio, a goal that seems tantalizingly close in light of the limited number of identified cases (approximately 2,000/year) and the few countries where the disease remains endemic (four).[66] The unique characteristics of poliovirus have presented significant challenges for further reductions in the incidence of the disease, despite laudable attention and investment in the effort, much of it supported by philanthropies including The Bill and Melinda Gates Foundation and Rotary International.[67]

The obstacles facing polio eradication have prompted some observers to suggest that a better overall strategy for global health is to maintain current levels of control while redirecting

the considerable resources (financial and personnel) going toward polio eradication campaigns to the many other causes of preventable morbidity and mortality worldwide.[68] A necessary and important debate has ensued among scientists, ethicists, and global health scholars.[69,70] The symbolic significance of disease eradication carries an allure that may not necessarily coincide with evidence-based approaches to global health policy. Since global health resources are limited, policymakers and funding sources should ensure that attention is directed to the prevention and treatment strategies that will prevent the most suffering and thereby do the most good.

Vaccines and pandemics

The 2009-2010 pandemic caused by a novel strain of H1N1 influenza provided a real-time test of global preparedness and planning for a potential influenza pandemic. While much of this planning had focused on the threat of H5N1 (avian) influenza, those preliminary activities provided an important foundation for the response to H1N1 influenza. Vaccines were central to these efforts.[71–74]

Within weeks of the identification of a potential pandemic strain of influenza in April 2009, the process of developing seed stocks for an eventual vaccine began.[75] The total time required to produce the first doses of vaccine adhered fairly closely to the long-predicted estimate of 6 months, underscoring the pressing need for new technologies to accelerate this process. Recognizing that vaccine doses would be limited in the initial weeks following their arrival, governments developed prioritization plans based on their earlier planning activities and epidemiologic evidence identifying the populations most severely affected by the pandemic strain. In the United States, the ACIP identified priority groups that ought to receive the vaccine first, including pregnant women, household contacts of infants younger than 6 months, health care workers and emergency personnel, children and young adults up to 26 years old, and older adults with underlying medical conditions.[76]

A robust outreach program by governments and public health officials ensured that the public was well informed about the nature of the threat and the precautions that should be taken short of receipt of a vaccine. These educational activities may have led to a peak in vaccine interest that preceded the arrival of sufficient doses to meet demand. By the time vaccine was widely available in late 2009, public interest had waned, in part owing to evidence showing the limited severity of the virus. In the United States, as many as 72 million unused doses of vaccine were scheduled to be disposed of at the end of the pandemic in 2010.[77]

The relatively mild nature of the 2009-2010 H1N1 influenza pandemic provided valuable knowledge and experience that ought to inform subsequent planning activities for public health emergencies in which vaccines may be available, including potential pandemics and acts of bioterrorism. As of late 2011, many reviews were underway to assess the successes and failures of the vaccination programs in the United States and worldwide. Among the topics being studied are the communication of accurate information about the severity of threats amid uncertainty, the efficiency of vaccine development, the adequacy of testing and postlicensure safety surveillance, the development of appropriate prioritization strategies, the structure of financing and distribution systems, and the allocation of vaccine to nations in the developing world. Each of these topics demands thoughtful review in preparation for future threats. Public health officials should aim to ensure that subsequent programs are designed to maximize benefits and minimize risks fairly among communities, populations, and nations.

It is essential that these reviews and subsequent revisions to planning strategies continue to include robust public dialogue, incorporating the perspectives and concerns of all constituencies that may be affected. As demonstrated in 2009, the urgency that follows the arrival of future threats will limit thoughtful discussion on these topics, making it all the more important to continue deliberation and planning in advance of public health emergencies. In particular, it is necessary to achieve and maintain public consensus on the rules that will govern allocation and rationing. Unless the rules are widely perceived as fair—arrived at by reasonable, open procedures—and just—helping persons at greatest risk while maximizing the public good—response plans are highly unlikely to succeed.

Conclusion: the future of vaccine ethics

The study of ethical issues in vaccination has received increasing attention in recent years, but there still have been relatively few concentrated attempts at broad exploration. Those attempts to examine vaccine ethics at a level larger than a single topic or debate have generated valuable results and can serve as models for future efforts.[78,79] A need continues to exist, however, for the creation of frameworks and key principles for ethical decision making throughout the vaccine life cycle. Such work would move us closer to solutions or consensus for many of the questions raised in this overview. These efforts would do far more good if they occur proactively, long before controversies or crises surface.

Advances in vaccination are attributable to gains in scientific knowledge, breakthroughs in research, and the creation of sound public health policy, among many other factors. Ultimately, however, the success of vaccination depends on maintaining widespread public trust, without which vaccination programs cannot succeed.[22] Preserving trust requires an unwavering awareness that the remarkable societal benefits of vaccination ultimately involve individual people who are entitled to respect, in a broad sense, that manifests itself at every point in the vaccine life cycle. By remaining sensitive and responsive to the consideration of ethical challenges, vaccination is best positioned to add to its history of public health triumphs.

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7. Grady C. Ethics of vaccines research. Nat Immunol 5:465–468, 2004.
22. Schwartz JL. Unintended consequences: the primacy of public trust in vaccination. Mich Law Rev 107:100–104, 2009.
45. Salmon DA, Teret SP, MacIntyre CR, et al. Compulsory vaccination and conscientious or philosophical exemptions: past, present, and future. Lancet 367:436–442, 2006.
47. Omer SB, Salmon DA, Orenstein WA, et al. Vaccine refusal, mandatory immunization, and the risks of vaccine-preventable diseases. N Engl J Med 360:1981–1988, 2009.
51. Colgrove J, Abiola S, Mello MM. HPV vaccination mandates: lawmaking amid political and scientific controversy. N Engl J Med 363:785–791, 2010.
53. Schwartz JL. HPV vaccination's second act: promotion, competition, and compulsion. Am J Public Health 100:1841–1844, 2010.
60. Poland GA, Tosh P, Jacobson RM. Requiring influenza vaccination for health care workers: seven truths we must accept. Vaccine 23:2251–2255, 2005.
68. Caplan AL. Is disease eradication ethical? Lancet 373:2192–2193, 2009.
73. Emanuel EJ, Wertheimer A. Who should get influenza vaccine when not all can? Science 312:854–855, 2006.
78. Feudtner C, Marcuse EK. Ethics and immunization policy: promoting dialogue to sustain consensus. Pediatrics 107:1158–1164, 2001.

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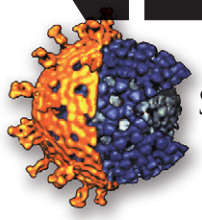

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Former Medical and Scientific Director
Pasteur Merieux Connaught (now Sanofi Pasteur)
Marnes-la-Coquette, France

WALTER A. ORENSTEIN, MD, DSc (Hon)
Professor of Medicine, Pediatrics, and Global Health
Emory University
Associate Director Emory Vaccine Center, Atlanta, GA
Former Deputy Director for Immunization Programs
Bill & Melinda Gates Foundation, Seattle, WA
Former Director, National Immunization Program, CDC
Atlanta, GA, USA

PAUL A. OFFIT, MD
Chief, Division of Infectious Diseases
Director, Vaccine Education Center
The Children's Hospital of Philadelphia
Professor of Pediatrics
Maurice R. Hilleman Professor of Vaccinology
Perelman School of Medicine
The University of Pennsylvania, PA, USA

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An imprint of Elsevier Inc.

First edition 1988, Second edition 1994, Third edition 1999, Fourth edition 2004,
Fifth edition 2008

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British Library Cataloguing in Publication Data
A catalogue record for this book is available from the British Library

ISBN-13: 9781455700905
Ebook: 9781455737987

Printed in China
Last digit is the print number: 9 8 7 6 5 4 3 2 1

Content Strategist: Sue Hodgson, Belinda Kuhn
Content Development Specialist: Joanne Scott
Content Coordinator: Sam Crowe
Project Manager: Julie Taylor
Design: Stewart Larking
Illustration Manager: Jennifer Rose
Illustrator: Oxford Illustrators/Ethan Danielson
Marketing Manager(s) (UK/USA): Carla Holloway