

# The Eradication of Infectious Diseases

## Understanding the Lessons and Advancing Experience

Stephen L. Cochi and Walter R. Dowdle

### Introduction

Humankind has always been fascinated by scourges of disease that cause incalculable misery in the world and have a devastating impact on society, and by subsequent attempts to eradicate such diseases (D. R. Hopkins 2009). The sustained eradication of an infectious disease agent, in which humans are the primary or sole host, was achieved for the first (and only) time in 1980, when the World Health Assembly declared the world free of smallpox, following a campaign that began in 1959 and lasted nearly twenty years. Success in eradicating smallpox worldwide led to an increasingly intensive examination of the concepts and definitions associated with disease eradication, and the development of general and specific criteria as predictors of success for particular candidate diseases. The *Carter Center International Task Force for Disease Eradication* initiated a formal review of candidate diseases in 1988 and is currently completing a second review. The criteria for eradication were comprehensively examined at a workshop in 1997 on “The Eradication of Infectious Diseases” (Dowdle and Hopkins 1998), followed in 1998 by an expanded global forum on “Disease Eradication and Elimination as Public Health Strategies” (WHO 1998; CDC 1999a).

More than a decade has passed since the basic concepts and issues of eradication were systematically addressed. Meanwhile, considerable experience has been gained through the initiatives to eradicate polio and dracunculiasis (guinea worm), as well as in efforts to eliminate such diseases as measles, maternal and neonatal tetanus, onchocerciasis (river blindness), and lymphatic

filariasis. Concepts of disease eradication have continued to evolve, influenced by scientific advances, field experiences, societal and ethical issues, and economic realities.

The need to convene this forum was especially timely since heightened interest in the potential eradication of various infectious diseases is once again moving front and center. For example, at the May 2008 meeting of the Executive Board of the World Health Assembly, the Board requested that WHO examine the feasibility of global measles eradication and report back to the Board in 2010. Also in 2008, both the WHO and the Bill & Melinda Gates Foundation publicly called for development of a program of work to achieve malaria eradication in the longer term (30+ years). These examples are illustrative of the ongoing fascination with the concept of eradication. However, they also demonstrate the continuing need to ensure that such initiatives are carefully considered, based on a full understanding of the biological, political, social, and economic complexities associated with a successful eradication program. With increasing interest in identifying candidate diseases for eradication, these complexities need to be addressed for the benefit of public health decision makers, politicians, scientists, and the world at large. In addition, the rapid accumulation of knowledge since the 1990s and the radical changes in the global landscape necessitate an in-depth, systematic reassessment and reexamination of eradication in the context of global health in the 21st century.

The central meeting of this *Ernst Strüngmann Forum* on “Disease Eradication in the Context of Global Health in the 21st Century” took place in Frankfurt, Germany, from August 29 to September 3, 2010. It brought together a diverse group of experts from academia, government and research agencies, international multilateral organizations, nongovernmental development organizations and foundations, the pharmaceutical industry, and the private sector. Participants were drawn from around the globe as well as from the many different disciplines that impact global health, including infectious disease, epidemiology, public health and preventive medicine, health economics, health policy and management, health systems research, and medical ethics.

Those who attended were acutely mindful that they were carrying on the legacy of those before them who have studied and discussed the concepts of disease eradication and grappled with its complexities. As Thomas Jefferson, in the early 1800s, wrote to Edward Jenner, the developer of the first smallpox vaccine: “Yours is the comfortable reflection that mankind can never forget that you have lived. Future nations will know by history only that the loathsome smallpox has existed.”

This Forum, through a combination of plenary discussions and focused small group deliberations on specific critical issues, conducted an in-depth, systematic reassessment and reexamination of eradication in the context of global health in the 21st century. The goals of this Forum were determined as follows:

- to assess the applicability, in the present and near-term future, of infectious disease eradication and elimination as components of the global health landscape;
- to explore the prospects, feasibility, and challenges of disease eradication/elimination initiatives; and
- to develop a framework for a priority-setting process to enable the identification of the most appropriate targets for disease eradication as well as the critical factors for success.

Lessons from previous and current eradication programs were examined, and the collective experience and knowledge of the Forum participants were used to extend global consensus on a variety of challenging issues. Each of four work groups focused on a specific set of issues as the central focus of their group discussions and reported back to the entire group. The scheduling permitted substantial opportunities for cross-fertilization through the participation and exchange of ideas across groups, an exchange that continued well after the final session in Frankfurt. Building on the progress achieved in Frankfurt, a follow-up meeting was convened in Boston from December 9–10, 2010, to expand the discussion on the critical components of the investment case for eradication and/or elimination initiatives.

### Evolution of Current Concepts and Definitions

The terms disease *eradication* and disease *elimination* describe ideal outcomes of disease control, where *control* is defined as the reduction of disease morbidity/mortality to a locally acceptable level (Fenner et al. 1998; Hinman 1984). The 1997 Dahlem Workshop attempted to better define the two terms by using current models and building on earlier definitions (Ottesen et al. 1998). Elimination was defined in two categories according to whether the indigenous agent remained (e.g., *Clostridium tetani*) or no longer remained (e.g., wild poliovirus) in the specific geographical area (Ottesen et al. 1998:48):

Elimination of disease: Reduction to zero of the incidence of a specified disease in a defined geographic area as a result of deliberate efforts; continued intervention measures are required. [The model was neonatal tetanus.]

Elimination of infection: Reduction to zero of the incidence of infection caused by a specific agent in a defined geographic area as a result of deliberate efforts; continued measures to prevent reestablishment of transmission are required. [The model was the 1994 declaration of the Americas as polio-free.]

The former was seen as the highest possible achievement for neonatal tetanus, the latter as a geographic step toward global polio eradication. The definition of eradication followed along the lines of common usage (Ottesen et al. 1998:48):

Permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts; intervention measures are no longer needed. [The model was smallpox.]

This definition of eradication implied a state of global permanence and conveyed the programmatic and economic advantages of eradication.

### **Events Since Dahlem**

In 1998, at the conference on “Global Disease Elimination and Eradication as Public Health Strategies” (WHO 1998; CDC 1999a) in Atlanta, some participants objected to the use of the term elimination, arguing that the distinction between eradication and elimination was artificial, confusing, not directly translatable in many languages, and not easily understood by people outside of international public health inner circles. The post-conference ad hoc group appointed to resolve the issue combined the two terms and defined eradication as (CDC 1999a:152):

The absence of a disease agent in nature in a defined geographical area as a result of deliberate control efforts. Control measures can be discontinued when the risk of disease importation is no longer present.

De Serres et al. (2000) noted that the Dahlem definition of elimination as “reduction to zero” was unrealistic and functionally unnecessary. They proposed to define elimination as a situation in which sustained transmission cannot occur and secondary spread from importation will end naturally.

In 2001, the anthrax attacks in the United States prompted some individuals to question publicly the concept of eradication, and the creation of opportunities for bioterrorism in increasingly nonimmune populations in a smallpox, polio, and possibly measles-free world. Since then, public concern over smallpox virus as an agent of bioterrorism has gradually subsided. However, allaying national security concerns over the phrase “intervention measures are no longer needed” is only possible for those parasitic diseases where agent eradication and extinction are synonymous.

In 2002, the national security debate was further stimulated by the report (Cello et al. 2002) that infectious poliovirus had been created in the laboratory following a recipe downloaded from the internet and using gene sequences from a mail-order supplier. Discontinuing intervention efforts, seen as justification for eradication in the smallpox model, became, in the views of some, justification for discontinuing disease eradication efforts, which ignores the “natural terrorism” of eradicable diseases that is the real threat to the world’s poorest populations on a daily basis.

However, if the geographical qualifiers are removed from the Dahlem definitions, as proposed by the Atlanta group in 1998, and if the intervention qualifiers are removed because of national security concerns, what remains of the

definition of eradication is: the absence of the disease agent in a defined geographical area as a result of deliberate control efforts.

This minimalist definition is not unlike that proposed by Andrews and Langmuir nearly fifty years ago as the “purposeful reduction of specific disease prevalence . . . to the point of continued absence of transmission within a specified area” (Andrews and Langmuir 1963:1). With this definition, elimination becomes redundant, national security becomes a non-issue, post-eradication intervention practices become optional according to the diseases and national policy, and eradication becomes national, regional, or global.

### **Definitions from This Forum**

The minimalist definition was dismissed by Forum participants on the grounds that it conveyed too little information. After much discussion during and after the Forum, the following definitions emerged:

*Global eradication:* The worldwide absence of a specific disease agent in nature as a result of deliberate control efforts that may be discontinued where the agent is judged no longer to present a significant risk from extrinsic sources (e.g., smallpox).

The major difference between this definition of eradication and the Dahlem version is that the proposed definition permits the post-eradication flexibility for national health authorities to consider on the basis of risk when control efforts may be discontinued.

*Regional or national eradication:* The absence of a specific disease agent in a defined geographic area as a result of deliberate control efforts that must be continued to prevent reestablished endemic transmission (e.g., polio, measles, rubella, guinea worm).

The context here assumes that the “defined geographic area” is substantially large and populous to give credibility to the claim that sustained eradication has been achieved.

*Elimination:* The absence of a disease caused by a specific agent in a defined geographic area as a result of deliberate control efforts that must be continued in perpetuity to prevent reemergence of disease (e.g., neonatal tetanus).

Most discussion at the Forum centered on use of the term elimination, particularly as a step toward global eradication. Some meeting participants expressed the opinion that the term elimination had been firmly implanted in the lexicon of the international health community, particularly in neglected tropical disease programs, and should therefore not be discarded. The measles group, for example, has stated on record that it prefers to reserve use of the term eradication exclusively for global achievements and the term elimination for subglobal (e.g., regional) geographic achievements (WHO 2010e). Other

meeting participants challenged the focus on established human diseases, and suggested that the definitions might exclude important accomplishments related to stopping emerging diseases, including the successful disruption of transmission of severe acute respiratory syndrome (SARS).

The intent of this Forum is not to establish a consensus document or exclusive definitions, but to identify shortcomings of the Dahlem definitions and offer possible solutions. Definitions are, and will continue to be, established through broad acceptance and popular usage.

## **Criteria for Disease Eradication Programs**

### **Biological and Technical Feasibility**

Although our definition of disease agents for eradication and elimination clearly included biological and technical feasibility, we emphasize the importance of these in the context of disease eradication programs. There are distinct biological features of an organism as well as technical tools and tactics that determine the potential eradicability of an organism (Hinman and Hopkins 1998; Aylward et al. 2000a; Dowdle 1998; Keegan et al. 2011). The categorization of a disease as not eradicable or difficult to eradicate can change completely if research efforts are successful in developing new and effective intervention tools. This demonstrates the central and important role of research in any eradication program. For purposes of this volume, we identified four indicators of primary importance:

1. An effective, practical intervention must be available to interrupt transmission of the agent.
2. Practical diagnostic tools must exist with sufficient sensitivity and specificity to detect levels of infection that can lead to transmission.
3. There must be an absence of a nonhuman reservoir (when humans are essential for the life cycle of the agent), and the organism does not amplify in the environment.
4. Success of the eradication strategy must be demonstrated in a large geographic area or region.

Past failures of eradication programs have been largely attributable to failure of the interventions or strategies, providing a cautionary note of the need to understand the natural history and biology of the disease thoroughly as a fundamental precept when considering an eradication or elimination program. For example, nonhuman primates were found to harbor yellow fever virus in 1915, and malaria mosquito vectors eventually became resistant to the insecticides (Aylward et al. 2000a). In the case of yaws, the prevalence and importance of inapparent infections were underestimated.

## **Societal and Political Support**

Despite strong biological, technical, and cost-benefit arguments for a particular eradication initiative, securing societal and political commitment is now recognized as a substantial challenge (Aylward et al. 2000b). An appreciation of societal and political considerations is critical in transforming eradication programs from technically feasible efforts into operationally successful initiatives (Hinman and Hopkins 1998; Aylward et al. 2000a; Dowdle 1998; Keegan et al. 2011; Aylward et al. 2000b; Henderson 1987; Cochi et al. 1998; Hall, this volume). The success of such initiatives is dependent on a consistently high level of political and societal commitment from the beginning to the end. Societal and political support in industrialized countries is also essential for mobilizing external resources for eradication in developing countries. Explicit efforts to identify countries with weak societal or political commitment must be central to evaluating the overall feasibility of any proposed eradication effort. Some of the key questions that arose during our discussions include:

- What organizational arrangements and institutional obligations are appropriate to disease eradication or elimination programs (see Stoever et al., this volume)?
- What are the most appropriate governance models (see Stoever, this volume)?
- What is the meaning of disease eradication or elimination to politicians, non-scientists, and others outside the health field (see Strebel et al., Bates et al., and Emerson, this volume)?
- What are the major political challenges in current eradication initiatives (see Hall, this volume)?
- What has been learned about political and community mobilization, and how do we build this into future eradication initiatives (see Bates et al., Pate et al., Hinman, Tyson and Biellik, Hanvoravongchai et al., all this volume)?

## **Economic Considerations**

Economic evaluations of health interventions play an increasing role in resource allocation decisions (Hall, this volume; Barrett 2004; Thompson and Duintjer Tebbens 2007; Duintjer Tebbens et al. 2011; Thompson and Duintjer Tebbens, and Thompson et al., this volume). Decisions have to be made as to whether the use of finite resources for a disease eradication or elimination program is preferable to their use in nonhealth sector projects, other health interventions, or direct investments in the overall health system. Formal economic analytical methods are not ideally suited to eradication programs; one of the most significant challenges relates to valuing the direct and indirect benefits of elimination nationally and eradication globally (Thompson and Duintjer

Tebbens, this volume). It can be difficult for politicians and the public to recognize the value of prevention and the savings associated with not incurring disease or treatment costs that an eradication program offers. These are global public goods.

Among the questions addressed at the Forum were the following:

- What are the critical components of the investment case for eradication and/or elimination initiatives (see Thompson et al., Walker et al., this volume)?
- Is there common ground for evaluating proposed eradication initiatives on economic and humanitarian criteria (see Thompson and Duintjer Tebbens, Thompson et al., and Walker et al., this volume)?
- Can a consensus be reached on the complexity and uniqueness inherent in applying economic principles to eradication programs (Thompson et al. and Walker et al., this volume)?
- Can humanitarian benefits be quantified (Thompson and Duintjer Tebbens, this volume)?

### **Linkage with Health Systems and Delivery of Other Health Interventions**

To be successful, eradication initiatives of the 21st century must balance the need for an obsessive, laser-like focus to achieve specific goals and objectives (D. R. Hopkins 2009) with a demonstration that such initiatives will positively interact with the broad-based, primary health care system (WHO Maximizing Positive Synergies Collaborative Group 2009; Melgaard et al. 1998; Atun et al. 2008; Taylor and Waldman 1998). Eradication and ongoing primary health care programs represent potentially complementary approaches to public health; areas of both synergy and tension exist that must be recognized and addressed. Efforts are needed to identify and characterize those factors that maximize positive interactions and minimize negative or harmful effects. Experience shows that negative effects are more likely to manifest themselves in countries where the health infrastructure is weak. A recent review encouraged “the creation of a new framework in which the disease-specific and health systems approaches are mutually interdependent and have a common goal to improve the health of all people” (WHO Maximizing Positive Synergies Collaborative Group 2009:2161). Questions that were addressed at the Forum included:

- What is the optimal use of resources for delivering additional health interventions in the context of disease eradication initiatives, and vice versa (Pate et al., Hinman, and Tyson and Biellik, this volume)?
- What are the mutual benefits of eradication initiatives and a functioning community health delivery system (Pate et al., Hinman, Tyson and Biellik, and Hanvoravongchai et al., this volume)?
- When do vertical (stand-alone) programs have a place in health systems (Hinman, this volume)?



## **Lessons from Previous and Current Eradication Programs**

A number of excellent reviews draw broad lessons from previous eradication program experiences that we find quite instructive when considering whether to embark on a specific disease eradication initiative (Hinman and Hopkins 1998; Aylward et al. 2000b; Dowdle 1998; Keegan et al. 2011; Aylward et al. 2000a; Henderson 1987). Hinman and Hopkins (1998) provided a list of ten main lessons from these collective experiences:

1. Understand the natural history of the disease thoroughly.
2. Consult widely before embarking on eradication.
3. Initiate surveillance early and use surveillance information to guide program strategy.
4. Eradication programs require a vertical approach.
5. Remain open minded and flexible; expect the unexpected.
6. Some countries may need more help than others.
7. Coordination of external donors is essential.
8. Political commitments from all levels are essential.
9. Inspire enthusiasm, but don't declare success prematurely.
10. Set a specific target date for eradication.

These general lessons are enriched by insights gained from comparative analyses of the successes and failures of previous eradication programs (Aylward et al. 2000b; Dowdle 1998; Keegan et al. 2011). A fundamental lesson is that neither biological nor technical feasibility—although essential, critically necessary elements of success—are sufficient criteria to be fulfilled in isolation. Additional nonbiological factors are ultimately the key to successful eradication efforts. Such evaluations have focused on political, social, economic, health system, leadership and management, and other factors that must be weighed as evidence for or against the establishment of an eradication initiative (Aylward et al. 2000b; Dowdle 1998; Keegan et al. 2011; Aylward et al. 2000a; Henderson 1987; Hall, this volume).

## **The Way Forward**

The issues addressed at this Forum illustrate how much has been learned and the wealth of experience gained over the past twenty years regarding the conception, formulation, planning, and implementation of various disease eradication and elimination programs. However, this Forum also illustrates the need for many more efforts to enlarge our knowledge base, experience, and understanding of this particular public health approach to conquering disease and human affliction. Eradication of disease is, in fact, the ultimate aspirational goal of public health; however, this powerful tool is potentially applicable to only a limited number of diseases in the current era. The history of past failed

eradication initiatives teaches us the critical need to exercise rigor and apply the lessons from these experiences as we contemplate embarking on new eradication or elimination programs. When considering such programs, nothing short of a systematic, comprehensive analysis of feasibility is needed, including a full examination of the challenges and opportunities of a decision to move forward, and the factors associated with likelihood of success or failure. This Forum describes the careful and deliberate evaluations that are required. When attributes and potential benefits are favorable, the way forward becomes clear.