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The principles and feasibility of disease eradication

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ABSTRACT

Smallpox eradication framed disease eradication as a monumental public health achievement in global health equity. The principles of disease eradication are encapsulated in a constellation of four conditions: biologic feasibility, adequate public health infrastructure, sufficient funding, and sustained political/societal will. Where the constellation exists, national eradication occurs in the absence of a global initiative. Assessing the feasibility of global eradication requires determining the constellation gaps for nations of all regions and identifying the human and financial resources to fill the gaps. The economic and humanitarian benefits of eradication have strong appeal. Global polio and guinea worm efforts are underway. Regional eradication of measles and rubella has been achieved in the Americas and other diseases have been proposed. Global decisions on disease eradication should include careful consideration of opportunity costs and prioritization of limited global health resources, with the objective of providing the most appropriate, cost-beneficial, and equitable outcome of disease control.

1. Introduction

Disease eradication provides global health equity, the highest aspiration of public health. Smallpox eradication framed disease eradication as a monumental global achievement with lasting societal and financial benefits with no need for continuing intervention measures [1]. More recent events suggest there may be more than one model, where national and regional eradication are seen as steps toward global eradication and continued intervention efforts may be optional [2]. In this manuscript we explore the evolution of definitions, principles, and feasibility of disease eradication and consider potential candidates.

2. The evolving definition of disease eradication

Eradication is defined in the Oxford (English) Dictionary and Thesaurus as a verb meaning to "root out, destroy completely, get rid of" [3]. Less agreement has been achieved on the term disease eradication as initially seen in the definitions of disease eradication proposed more than 45 years ago by Soper [4] and a year later by Andrews and Langmuir [5]. The primary differences between the two are that eradication is "global" (Soper), with the implied economic benefits of discontinued preventive measures or "within a specified area" (Andrews and Langmuir), without reference to discontinuation of intervention measures. Soper's definition gained acceptance with the global declaration of smallpox eradication in 1980. The term elimination became increasingly used to describe the "*absence of transmission within a specified area*". Further modifications of the basic Soper definition were proposed by Hinman [6] and the International Task Force for Disease Eradication [7].

The 1997 *Dahlem Workshop on the Eradication of Infectious Diseases* attempted to define elimination and eradication more precisely using current models and building on earlier definitions [8]. Eradication was defined as: "*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.*" Smallpox was the model. Elimination was defined separately for disease (neonatal tetanus) and infection (poliovirus). The key differences from eradication were the terms "*in a defined geographic area*" as opposed to "*worldwide*" and that "*continued measures to prevent reestablishment of transmission are required*". The model for the latter was the 1994 declaration of the Americas as polio-free.

In 1998, at the *Conference on Global Disease Elimination and Eradication as Public Health Strategies* in Atlanta, objection was voiced to legitimatizing the term elimination, claiming the distinction between eradication and elimination was artificial and a post conference ad hoc group was appointed to combined the two terms [9].

In 2001, the anthrax attacks in the United States renewed concerns about the vulnerability of smallpox-naïve populations and raised questions about disease eradication as creating opportunities for bioterrorism. Proof that bioterrorism will never be a security

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threat is possible only for parasitic diseases (i.e., guinea worm) where eradication and agent extinction are synonymous. National security concerns were reinforced by the report of Cello et al. in 2002 that infectious poliovirus could be created in the laboratory [10]. In the views of some, cessation of intervention efforts, once seen as justifying eradication, became justification for discontinuing eradication efforts.

However, the "national security" focus fails to address the issue of "human security" and the reality that the largest global source of biological risk continues to be naturally occurring infections [11]. Further, continuing disease intervention efforts after eradication remains an individual national option, provided the intervention tool itself does not constitute a potential threat; for example, oral poliovirus vaccines (OPV) must be replaced with inactivated polio vaccines (IPV) to avoid generating circulating OPV-derived viruses. However, if the geographical qualifiers are removed from the Dahlem definitions as proposed by the Atlanta group and if the intervention qualifiers are removed because of national security concerns, the basic definition of eradication becomes:

> "The absence of the disease agent in a defined geographical area as a result of deliberate control efforts."

With this basic definition, post eradication intervention practices can differ according to disease and national policy and eradication can be defined in a *global, regional, or* national context, assuming the sub-global areas are substantially large and populous to give credibility to the claim that sustained eradication has been achieved.

Current definitions were reviewed at the Ernst Strüngmann Forum on Disease Eradication in the Context of Global Health in the 21st Century, in September 2010, shortly after the conclusion of the Smallpox Eradication Symposium. Opinions were expressed that any definition of global eradication should include the option of discontinuing the intervention. Others supported continued use of the term elimination for national and regional milestones, particularly in neglected tropical disease programs. The measles group, for example, prefers to reserve use of the term eradication exclusively for global achievements and the term elimination for regional or national geographic achievements [12]. The proceedings of the Strüngmann Forum are scheduled for publication by MIT press in the near future. The purpose of this manuscript is to draw attention to events that impact the current disease eradication definitions and to offer possible solutions. Definitions will continue to evolve through common usage.

3. The principles of eradication

The constellation of conditions that make eradication of infectious diseases feasible is well established:

- Biologic feasibility (including safe and effective intervention measures, whether drugs, vaccines, or clean environment)
- Adequate public health infrastructure (including management and operational capacity)
- Sufficient funding
- Sustained political/societal will (including all levels from the community to the national government)

National eradication can occur as a sustained outcome of good public health practice where the constellation exists, often without eradication as the stated goal. More than 85% of countries had eradicated smallpox by the time the initiative became fully operative in 1967. More than one third of the world's countries had eradicated polio by the time the initiative began in 1988. India eradicated yaws in 2006 [13].

Regional eradication in its simplest sense is achieved through assisting all remaining endemic countries in the region to fill the gaps in the disease-specific constellation, which may include, for example, international assistance to purchase vaccines and to supplement/strengthen health infrastructure. The American Region eradicated measles in 2002 and rubella in 2009 [12] [also see paper in this supplement]. WHO regions vary widely in the number of countries requiring assistance and in the fluidity and size of gaps to be filled.

Global eradication in its simplest sense is achieved through assisting all remaining endemic WHO regions to completely fill the gaps in the disease-specific constellation, requiring the full commitment of the global community to provide the financial and technical resources to achieve the goal.

The attractions of global eradication initiatives are multiple:

- Is the ultimate endpoint among public health goals
- Positive benefit–cost analyses (smallpox, polio, measles, rubella)
- Appeals to donors (clear and measurable goals, finite time frame)
- Advances a culture of prevention
- Improves acceptance of other disease/health interventions
- Builds health infrastructure and program experience
- Provides social justice and health equity worldwide

On economic grounds, the benefits of eradication remain strong relative to the high cost of long term control [14,15]. Current examples of the cost of control are the large 2010 polio outbreak in Tajikistan with 458 laboratory-confirmed cases of paralytic disease and the 2009–2010 outbreaks resulting from importations into 21 previously polio-free countries in Africa [16]. The question has been raised whether high levels of control are ever economically justifiable if eradication is feasible [17].

On humanitarian grounds, health equity is a powerful motivating force in support of eradication. Yet fundamental to achieving health equity through disease eradication are careful considerations of opportunity costs and prioritization of limited global health resources. The goal is not eradication per se, as attractive as that may be, but to achieve the most appropriate, cost beneficial, and equitable outcome of disease control [18,19].

4. The feasibility of national/regional/global eradication

The history of early eradication efforts and the question of when a disease is eradicable have been addressed in multiple publications [18–20]. Socio-political commitment and feasibility are as important as biologic and technical feasibility [20]. The human element (political and societal will) has proved a key component in every initiative, with local challenges of apathy, cultural traditions, religious beliefs, and civil strife. Eradication success depends on the support of political leaders at all levels, including the community, local program management, employees, and volunteers. Ultimately, all eradication, like all politics, is local.

Crucial questions to be addressed at the local community level include whether the initiative will:

- have the sub-national and local leadership support to honor the national commitment
- provide additional community benefits where locally the disease has low priority
- achieve synergies in delivery of health interventions to address the multiple health objectives and needs of local communities
- build sustainable improvements in health infrastructure

Strong public health (horizontal) programs facilitate success of eradication (vertical) initiatives [21].

Assessing feasibility of global disease eradication is a dynamic process. Even the most thorough feasibility assessment may not identify all challenges that may arise once the initiative has begun. Cumulative experiences from malaria, smallpox, polio, and guinea worm have shown strong, ongoing research programs to be essential. Successful rinderpest eradication, as for smallpox, is attributed to an evolving immunization strategy based on initiative-driven epidemiologic research [22].

Research in the Global Polio Eradication Initiative has included the search for new tools and innovative methods to improve surveillance, management, staff performance, monitoring and evaluation strategies, and provide value to routine tasks [23]. Behavioral/social research findings have been crucial for understanding community priorities and providing evidence-based communication strategies to overcome sociocultural or religious beliefs and increase immunization acceptance among the migrant, underserved and hard-to-reach populations [24]. Continuing research on improved eradication tools and strategies is essential [25]. Real-time mathematical modeling addresses economic issues and complex programmatic dynamics [26].

5. Candidates for disease eradication

> ". . .. eradication is a powerful tool that is only rarely applicable. It should be asserted and used with great care, after much thought, and ideally with broad consensus and endorsement by the World Health Assembly." [27]

In addition to the current global eradication initiatives declared for polio and guinea worm, the International Task Force for Disease Eradication proposed diseases (updated in 2008) with eradication potential to include measles, rubella, cysticercosis, lymphatic filariasis, and mumps [7]. Diseases not on the Task Force list, but proposed by others include malaria, onchocerciasis, and yaws.

Whether the time is ripe for a World Health Assembly (WHA) resolution on the eradication of measles/rubella is a current topic of discussion in the international community [see measles and rubella paper, this supplement]. In opposition are concerns pertaining to current economic conditions, other immunization priorities, political will and, interestingly, the current success of the accelerated measles reduction efforts even in the absence of an eradication resolution. In favor of a resolution are the benefit–cost analyses that consistently support measles/rubella eradication (Levin et al. J Infectious Dis 2011 [in press]), the view that a second immunization initiative could actually benefit and sustain polio eradication and improve routine childhood vaccine coverage, and that a global initiative would continue the present momentum in measles/rubella reduction, particularly in Africa.

Debate is also seen on the need for WHA resolutions in the near future for the longer-term candidates such as onchocerciasis, lymphatic filariasis, and malaria. On one hand is the concern that a premature WHA resolution in terms of knowledge, technical feasibility, and timing could over promise and set back steady global progress. On the other hand, a WHA resolution to establish a global goal, at whatever time in the future, could be an important step to stimulate basic and operational research efforts in otherwise neglected diseases, legitimatize long-term planning, and provide national and regional guidance. Whatever the outcome of the debate, there is consensus that never again should the world allow research and control on important global diseases to languish to the degree that it did for malaria since the eradication effort was abandoned in 1957.

A WHA resolution on eradication is important. It provides the license and establishes a collective goal for all nations. But a WHA resolution has not always immediately translated into national or WHO actions. Ministers of health may not have full commitment of their governments, governments change, WHO staff members have other responsibilities, and funding may not be immediately forthcoming.

Global eradication initiatives require strong, adaptive, global coordination and, as seen in the eradication of smallpox and rinderpest, a critical mass of committed public/private consortia and tireless organization and individual champions to provide conscience, passion, and leadership, without which the initiative will not succeed.

6. Conclusions

In 2010, the world celebrated 30 years of freedom from the virus of smallpox and the need for a vaccine. The principles of disease eradication are encapsulated in a well-established constellation of four conditions. Where the constellation exists, national eradication occurs in the absence of a global initiative. Advancing from national to global eradication requires identifying and filling the constellation gaps for nations in all regions. Active global central coordination is essential, but all eradication is ultimately local. Most challenging is the human element, assuring sustained political will and societal support at all levels. The economic and humanitarian benefits of eradication have strong appeal. Global polio and guinea worm efforts are underway. Regional eradication of measles and rubella has been achieved in the Americas and other diseases have been proposed. Global decisions on disease eradication should include careful consideration of opportunity costs and prioritization of limited global health resources, with the objective of providing the most appropriate, cost-beneficial, and equitable outcome of disease control.

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