Eradicating pathogens
The human story

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Eradicating human pathogens is a young science, and there is still much to learn about its role in controlling existing and emerging diseases

The allure of eliminating diseases forever through eradicating their causative organisms no doubt tantalised physicians and politicians even before germ theory changed the course of medicine and public health profoundly in the 19th century. Only when William Crawford Gorgas, a major general in the US army and a surgeon, embarked on the ill fated quest to eradicate yellow fever from the jungles of Panama in 1915,[1] however, did someone actually try to test the theory. Although Major General Gorgas had to abandon the dream of a world rid of yellow fever, he did leave behind concepts that continue to underpin the practice, and politics, of eradication today.[2]

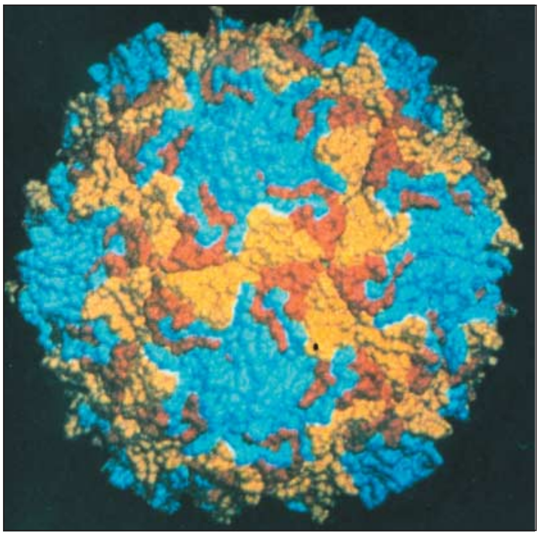
First attempts were unsuccessful

Yellow fever was the first of six diseases targeted for eradication during the 20th century. The eradication programme for yaws soon followed, but by 1967 this had also failed.[3] The massive effort to eliminate malaria from 1955 to 1969 was not only unsuccessful but is sometimes accused of resulting in a dramatic rebound in numbers of cases in many countries.[4] Consequently, by the second half of the 20th century, the seductive sheen of eradication had dulled considerably.[5] Despite the 100% failure rate of the first three efforts by the late 1960s, the concept of eradication as a public health goal was not completely discredited; rather, the foundation was laid for a more scientific assessment of the biological and operational feasibility of eradicating other pathogens.[1 2]

The yellow fever eradication effort was stopped because of the discovery of a non-human (monkey) host from which the virus was being reintroduced into human populations. Yaws eradication showed the fundamental importance of a surveillance strategy capable of detecting both clinical and subclinical infections. The malaria programme reinforced the need for tools that could rapidly interrupt human to human transmission anywhere, as well as the enormous concentration of resources needed to eliminate a pathogen worldwide. All three initiatives highlighted the need to prove the technical and operational feasibility of eradication on a large geographical scale before launching a global effort.

Success at last

After three consecutive eradication failures, the fourth eliminated a disease that, although already unknown to today's medical students, killed 2-3 million people a year as recently as 1967—almost as many as AIDS killed in 2004.[6] Smallpox eradication also paid an extraordinary return on investment: the entire $100m (£58m; €86m) in external financing that was required to help countries where smallpox was endemic to eradicate the disease is recouped every 26 days.[7] Innumerable lessons were learnt, ranging from the technical and logistical aspects of eradication to societal and political ones.[8]



GLOBAL POLIO ERADICATION PROGRAMME

The wild polio virus up close

Ongoing eradication efforts

The fifth and sixth global eradication efforts were launched in 1986 and 1988 and are ongoing; they target dracunculiasis (a painful, debilitating disease also known as guinea worm) and poliomyelitis, respectively.[2] The principle risk to the successful conclusion of these programmes is quite different from the technical problems that plagued the first three eradication efforts; the common challenge for the eradication of polio and guinea worm is sustaining the tremendous political and societal will needed, in endemic countries and donor countries, to implement and finance eradication activities successfully in the face of disappearing diseases.

When is eradication a possibility?

By the close of the 20th century, nearly 100 years of experience with six eradication efforts had coalesced into a framework of three major criteria for assessing the "eradicability" of other organisms.[9-10] First, eradication had to be biologically and technically feasible. In general this meant that there should be no non-human host capable of sustaining transmission of the causative organism and no chronic carrier state; simple tools and strategies would need to exist for diagnosing and interrupting human transmission. Secondly, eradication of the target organism should be cost effective; the tremendous marginal costs of moving from high level control or regional elimination to global eradication should be recoverable in the medium term through direct savings, such as those associated with foregone treatment and control costs. Thirdly, sufficient political and societal will would be needed to sustain such a massive undertaking over several years (a criterion that by its very nature is almost impossible to confirm in advance).

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By 1999, general principles had also emerged for reconciling the maddening confusion of definitions. These principles helped to differentiate the control of an organism (with continued disease and control measures) from its elimination (absence of disease but requiring continued control measures), eradication (global elimination such that control measures could stop but that could require bio-containment of stocks), and extinction.[11]

A recent success

Very early in the 21st century, new knowledge was already informing these concepts as an alarming new disease went from discovery to worldwide elimination in a remarkable nine months through the international application of classic public health measures. Although the severe acute respiratory syndrome (SARS) may yet re-occur or re-emerge from a non-human reservoir,[12] its worldwide elimination showed that extraordinary political and societal support could sustain a massive, coordinated, public health effort long enough to interrupt transmission of an organism globally. Interestingly, the biological and technical feasibility of SARS elimination was at best speculative at the outset of that effort (no diagnostic test even existed when it first emerged).

Conclusions and outlook

As this brief account shows, the "science" of eradication is still very young, and much is still to be learnt. Eradication may, for example, be not only an appropriate goal in disease control for some ancient scourges but the preferable goal to control some new pathogens rapidly. This should not be lost in the debate that always surrounds eradication because the window of opportunity for eliminating a disease globally can be very narrow (smallpox eradication may not have been possible in the HIV era because of the risk of fatal adverse events following the immunisation of infected individuals). Beyond polio and guinea worm, the current list of potentially eradicable human pathogens is quite short. That list includes measles, however, a disease that killed as many children as HIV in 2000.[13] Measles, for which diagnosis is cheap and simple, has already been eliminated from large geographical areas by using a vaccine that costs just $0.17 per dose.[14]

Although the eradication of human and animal pathogens have many parallels, joint work has to date been limited to the sharing of experience and best practices in areas such as strategic approach, surveillance and certification, and advocacy and mobilisation of resources. With the UN Food and Agriculture Organisation's global rinderpest (cattle plague) eradication programme (GREP) now showing that eradication of an animal pathogen may indeed be feasible[15] and the emerging importance to both humans and animals of pathogens such as avian influenza, it is intriguing to consider the possibility of joint eradication programmes in the future. The likelihood and success of any future eradication initiative will, however, depend on first securing and then sustaining a level of international consensus and support that no eradication effort, whether against a human or animal pathogen, has yet to enjoy.

Competing interests: None declared.

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The animal story

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The UN Food and Agriculture Organisation's global rinderpest eradication programme (GREP)—the first and only attempt to eradicate an animal pathogen—provides several learning points from the veterinary perspective

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Rinderpest is (was is possibly more accurate) an ancient disease of cattle, believed to have been the origin of human measles,[1] caused by an epitheliotropic and lymphotropic morbillivirus. Characterised by high fever, ocular and nasal discharges, dysentery, and dehydration it can cause death in up to 100% of cattle, water buffaloes, and yaks. Many wild ungulates are also highly susceptible, but not humans. Not surprisingly, it was the dread of farmers throughout the European, Asian, and African continents for centuries, even millennia. Sweeping west, east, and south out of central Asia, this devastating disease changed the course of history, following in the wake of marauding armies bringing death and devastation that contributed to the fall of the Roman empire, the conquest of Europe by Charlemagne, the French revolution, the impoverishment of Russia, and the colonisation of Africa.[2] Having been defeated in Europe by 1928, it was the subject of intensive eradication effort in Africa and Asia for most of the last century, yet not until 1993 was a programme mounted by the Food and Agriculture Organisation of the United Nations to bring about