Emerging, evolving, and established infectious diseases and interventions

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Planning, implementing, and evaluating interventions against infectious diseases depend on the nature of the infectious disease; the availability of intervention measures; and logistical, economic, and political constraints. Infectious diseases and vaccine- or drug-based interventions can be loosely categorized by the degree to which the infectious disease and the intervention are well established. Pertussis, polio, and measles are three examples of long-known infectious diseases for which global vaccination has dramatically reduced the public health burden. Pertussis vaccination was introduced in the 1940s, polio vaccination in the 1950s, and measles vaccination in the 1960s, nearly eliminating these diseases in many places.

Many known infectious diseases tend to be epidemic, but exactly when and where these epidemics will occur is uncertain. For such sporadic infectious diseases, it may be most efficient to implement a reactive vaccination campaign once an outbreak has begun. Planning for reactive vaccination requires keeping a mobile vaccine stockpile available that can be quickly moved for emergency vaccination. This strategy could be used for epidemic cholera, such as occurs in parts of Africa (1). When cholera was introduced into Haiti in 2010, such a stockpile did not exist. Limited supplies of cholera vaccine were scattered in different locations, and a decision was made not to vaccinate the local population, even though mathematical models showed that with limited quantities of vaccine, concentrating vaccination in high-risk areas would be most efficient (2). Now that such a stockpile of 2 million doses of oral cholera vaccine exists (3), it can be used for future cholera epidemics. Mobile stockpiles, such as the oral cholera vaccine, often have a finite shelf life, and their use can be valuably reassembled in endemic locations, such as Bangladesh, that experience annual cycles of high incidence.

For long-term intervention strategies, sustainability is an issue, and strategies can change as the economic constraints change or as new products become available. For example, a new product against meningococcal A meningitis was developed that overcame the reactive vaccination strategy in the meningitis belt of sub-Saharan Africa. An international commitment working through the Meningitis Vaccine Project developed an inexpensive vaccine against meningitis A (4) that can be used in proactive vaccination.

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References and Notes


4. Evidence Aid Priority Setting Group, PLOS Curr. 5, 10.1371/ current.dis.5cf6d8887633409f8d2d864e20c31 (2013).


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evaluate not only the direct effect of vaccination, but also the indirect and overall effects. In all instances, good field epidemiology and surveillance are required.

**Changing fronts**

Even when a good intervention is available, problems can arise, requiring ongoing careful epidemiological assessment of apparently excellent interventions. Interventions can put selective evolutionary pressure on pathogens, resulting in drug resistance and immune escape. The emergence of drug-resistant strains such as methicillin-resistant *Staphylococcus aureus* (MRSA) and multidrug-resistant tuberculosis, as well as drug-resistant malaria parasites, is the result of evolutionary pressure. The United States is experiencing a resurgence of pertussis cases, despite high coverage and booster vaccination of teenagers. The reasons are poorly understood, but it is possible that the current acellular pertussis vaccines do not produce long-lasting immunity (16). In addition, pertussis strains that lack one of the important vaccine antigens have evolved because of immune escape and have spread in recent years (18). Careful epidemiological assessment of the changing pertussis situation is required to guide development of new vaccines and intervention strategies (16).

Influenza viruses evolve antigenically over time, escaping both natural and vaccine-induced immunity. Challenges arise from producing an influenza vaccine each year, and constant monitoring of the influenza viruses is needed. Global influenza virological surveillance has been conducted through the World Health Organization’s (WHO) Global Influenza Surveillance and Response System for more than half a century. Twice a year—one for the Northern Hemisphere and once for the Southern Hemisphere—the WHO advisory panel decides what viruses will be incorporated in the next seasonal influenza vaccine (17).

Although global vaccination has eliminated polio in many parts of the world, choosing between live-attenuated oral polio vaccine (OPV) and inactivated polio vaccine (IPV) is a crucial policy decision once elimination has been achieved. OPV is less expensive and easy to administer; can be transmitted to close contacts and in the environment, helping to spread vaccination; and induces more natural immunity in the gut, preventing onward transmission. However, OPV can revert, causing very occasional cases of polio. IPV is more expensive, but it induces the production of antibodies that can prevent paralytic disease. IPV does not induce gut immunity and thus does not prevent onward transmission, but it also does not raise the same safety concerns as OPV. When polio has been essentially eliminated and the vaccine is affordable, then the switch to IPV from OPV is a sensible policy decision. However, this choice can also be fraught with difficulties. Israel switched to IPV for 9 years, but through intense environmental surveillance discovered circulation of type 1 wild poliovirus and thus reintroduced OPV (18, 19). This excellent environmental surveillance facilitated the rapid response to the changing situation.

The shifting landscape of infectious diseases and interventions poses challenges. Focused field epidemiology and surveillance are needed to provide the information required to make informed policy decisions about interventions to further global public health.

**Fig. 2.** Mass cholera vaccination is more cost-effective when overall protection is considered compared with calculations that only account for direct protection. According to WHO convention, the ratio of program cost to DALYs averted in a cost-effectiveness analysis is classified by the per capita national gross domestic product (GDP) of the country of interest: Less than the GDP per capita classifies an intervention as very cost-effective; between one and three times the GDP per capita is cost-effective; and more than three times the GDP per capita is cost-ineffective (21). [Courtesy of C. Troeger and D. Chao]

**Cost-effectiveness of cholera vaccination**

Cost per DALY averted

<table>
<thead>
<tr>
<th>Vaccination coverage (percent)</th>
<th>Not cost-effective (&gt;=$2487/DALY averted)</th>
<th>Direct protection</th>
<th>Cost-effective (&lt;=$2487/DALY averted)</th>
<th>Overall protection</th>
<th>Very cost-effective (&lt;=$829/DALY averted)</th>
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**REFERENCES AND NOTES**


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