Epidemiology of Transmissible Diseases after Elimination

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Elimination of an infectious disease is often understood to mean the total absence of cases in a population. This situation can occur only if the entire population is immune as a result of either natural disease or vaccination. However, this costly and unrealistic scenario is not necessary to ensure elimination, more appropriately defined as a situation in which sustained transmission cannot occur and secondary spread from importations of disease will end naturally, without intervention. The authors describe the size and duration of outbreaks caused by imported infections after indigenous transmission has been eliminated. They show that the status of the elimination process can be monitored by assessing the proportion of cases imported and the distribution of outbreak sizes. Measles in Canada, the United States, and the United Kingdom provides a good example of the relevance of these criteria. Surveillance of the size and duration of these outbreaks enables maintenance of elimination to be monitored. Am J Epidemiol 2000;151:1039-48.

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Many countries are trying to eliminate vaccine-preventable infectious diseases such as polio, measles, and rubella. In lay language, elimination of a disease means a total absence of cases. The 1997 Dahlem workshop on eradication of infectious diseases defined elimination of disease as "the reduction to zero of the incidence of a specified disease in a defined geographical area as a result of deliberate effort; continued intervention measures are required (1, p. 23)." Assessment of elimination status appears easy with this criterion. However, use of this criterion means that elimination could not be achieved without global eradication. Until then, importations from countries with less-effective disease control are likely to produce some secondary spread among susceptible persons, so a complete absence of cases could occur only if all persons were immune.

This goal is impossible to achieve. Recent statements about elimination have recognized that some cases secondary to importation will occur and that the objective is to prevent indigenous transmission (2). However, indigenous transmission is not defined clearly: is it transmission of the disease to a resident by an imported case; is it the secondary transmission from that first resident case to other residents; or is it transmission by the second, third, or fourth generation of resident cases? At what point does limited secondary transmission become sustained transmission? The US measles elimination program in the late 1970s...
and early 1980s categorized cases as indigenous if they occurred more than two generations after an importation (3).

To better define elimination of disease, this paper reviews the basic concepts of transmission and explores qualitative and quantitative differences in the epidemiology of communicable disease before and after elimination has been achieved. In particular, we calculate the expected size and duration of outbreaks caused by imported infections. We discuss how such outbreaks should be interpreted in the context of an elimination strategy and present simple criteria that can be used to assess the status of the elimination process in a population. To illustrate the relevance of our approach, we review the epidemiology of measles in Canada, the United States, and England and Wales.

**BACKGROUND**

Transmission of an infection within a population depends on its infectivity and duration, the contact rates between persons in a society, and the susceptibility of those persons to the infection (4). The combined effects of these variables can be summarized by the effective reproduction number $R$, defined as the average number of secondary cases produced by a typical case in that particular population. When $R$ is greater than 1, the number of cases increases from one generation of cases to the next; when $R$ is less than 1, the number of cases decreases. Thus, the epidemic threshold is defined by $R = 1$ (5).

### Endemic infection

The $R = 1$ threshold defines the endemic equilibrium state at which each infection produces one secondary infection. In the absence of a control program, some infections, particularly those that do not confer immunity and those for which there is a carrier state, tend to occur in this steady equilibrium state. In contrast, acute infections that confer immunity (e.g., measles) tend to exhibit epidemic cycles. During an epidemic cycle, $R$ oscillates around the threshold at $R = 1$, changing constantly as the level of susceptibility fluctuates. An epidemic can begin if $R$ is greater than 1. After the onset of an epidemic, $R$ begins to decline as the number of susceptible persons falls, because infected persons acquire immunity. When transmission has sufficiently depleted the pool of those who are susceptible, $R$ is reduced to less than 1 and the number of cases declines. At the end of the outbreak, $R$ begins to rise again because new susceptible persons are added through birth (figure 1). When $R$ exceeds 1, a new epidemic can begin. If a population is sufficiently large, chains of transmission can be sustained throughout the period during which $R$ is less than 1; otherwise, an epidemic will not occur until the infection is reintroduced to the population. Indigenous transmission (endemicity) will be eliminated if $R$ is maintained constantly under the epidemic threshold (figure 1).

### Elimination

The fact that $R$ is under the elimination (epidemic) threshold does not mean that everyone is immune but...
that the proportion of susceptible persons is sufficiently low that sustained transmission is impossible. If this situation is maintained, endemic transmission will stop eventually. Imported cases will drive the observed epidemiology by producing some limited secondary spread in the few persons still susceptible. Elimination should therefore be defined as a situation in which endemic transmission has stopped, sustained transmission cannot occur, and secondary spread from importations will end naturally, without intervention. While \( R \) must be less than 1 to prevent sustained transmission, there is no particular value of \( R \) at which elimination is achieved; it is the constant maintenance of \( R < 1 \) that defines elimination.

The best way to monitor the status of the elimination process in a population is to estimate the value of \( R \) in that particular population and to follow closely its evolution over time. \( R \) summarizes the susceptibility of the population, its mixing patterns, and the contagiousness of the disease. It can be assessed directly by interpreting serologic surveillance data with mathematical models if there is a good serologic correlate of protection (6). Alternatively, or in the absence of a correlate, it can be estimated indirectly by assessing the epidemiologic impact of imported cases. In this paper, we look at this impact from different perspectives to enable different criteria to be developed.

CRITERIA FOR ASSESSING ELIMINATION

Criteria for assessing the status of an elimination program are developed by investigating the epidemiology of infection after elimination has been achieved. We therefore assume at the outset that \( R \) is less than 1 and that infection has been eliminated from the population. In this situation, we look for ways to estimate the value of \( R \) from outbreak data.

Proportion of cases imported

If endemic transmission has been eliminated from a population, all cases occurring in that population must be linked to an imported infection. As \( R \) is the average number of secondary cases produced by a typical case, the imported case infects on average \( R \) others to form the first generation of cases. In turn, each of these \( R \) cases infects \( R \) persons, leading to \( R \times R = R^2 \) cases in the second generation, and so on. The total outbreak size is the sum of cases in all generations, including the imported case. The average number of cases \( (A) \) arising from an importation, including the imported case and all subsequently linked persons, can be estimated by using the following geometric progression: \( A = 1 + R + R^2 + R^3 + \ldots \), where 1 is the imported case, \( R \) is the number of persons infected by the imported case, \( R^2 \) is the number of persons infected by the first generation of cases, \( R^3 \) is the number of persons infected by the second generation of cases, and so forth.

This expression depends on two assumptions: first, the depletion of susceptible persons can be ignored; second, mixing is random. The first assumption is reasonable in the context of urban outbreaks but not, for instance, with school or household outbreaks. The second assumption, while not fully justified, provides a simple framework for investigating the key ideas involved.

When \( R \) is less than 1, the geometric progression for the average number of cases originating from 1 case sums to give \( A = 1/(1 - R) \). For example, if \( R \) equals 0.9, the introduction of 1 imported case will generate an average total of 10 cases (the primary case and 9 secondary, tertiary, etc., cases).

One method for assessing the value of \( R \) is to calculate \( A \) directly from only those outbreaks in which the imported primary case has been identified. However, doing so would discard much information since, after elimination, all outbreaks must be linked to an imported case. Thus, 1 in every \( A \) cases is imported; hence, the proportion of imported cases is \( I/A = 1 - R \). Use of this equation provides a simple way to estimate \( R \) in populations in which \( R \) is less than 1 (7): \( R = 1 - \) the proportion of cases imported. This method will overestimate \( R \) if imported infections (particularly those in visitors) are less likely to be reported than those acquired locally, which is especially true for short-stay visitors who may even have left the country before developing symptoms.

Distribution of outbreak sizes

The distribution of outbreak sizes arising from an importation is also of interest. To investigate this, we modeled the spread of infection by means of a branching process (8) (refer to the Appendix). When this model is used, the expected distribution of outbreak sizes can be calculated (figure 2). For example, the probability that an importation will lead to an outbreak involving five or more cases with \( R \) equal to 0.9, 0.8, 0.7, and 0.5 is 31, 25, 19, and 8 percent, respectively. The probability that an importation will produce an outbreak involving at least 25 cases is 8.7, 3.7, 1.1, and 0.2 percent given the same values of \( R \).

If data were complete, the distribution of outbreak sizes could be used to estimate \( R \) from the results shown in figure 2. However, it is probable that larger outbreaks are more likely to be reported than single cases. Focusing on outbreaks larger than a
Some underreporting of the number of cases involved in individual outbreaks is likely, particularly because of unrecognized links in the chain of transmission. Such underreporting would lead to an underestimation of the value of $R$. 

given size may reduce this bias. For example, the distributions for outbreaks involving at least three and at least five cases are shown in figure 3. These distributions provide a second method for estimating the value of $R$. 

FIGURE 2. Distribution of the size of outbreaks of disease resulting from an importation, according to the reproduction number.

FIGURE 3. Top: distribution of the size of disease outbreaks of at least three cases resulting from an importation, according to the reproduction number. Bottom: distribution of the size of disease outbreaks of at least five cases resulting from an importation, according to the reproduction number.
Distribution of the duration of outbreaks

The model can also be used to assess distribution of the number of generations of transmission (figure 4). The probability that an imported case will cause three or more generations of secondary cases is 31 percent if $R$ equals 0.9 and 19 percent if $R$ equals 0.7. Thus, if $R$ is less than 1 and many importations occur each year, the occurrence of secondary cases may mimic a low level of endemicity.

The distribution of the number of generations of spread provides a third way of estimating $R$. The duration of an outbreak may be less prone to bias from underreporting than the number of cases, but it may be difficult to determine the number of generations of transmission. However, there is a potential to allow for missing links in the chain of transmission. For example, it might be reasonable to assume that two cases in the same town whose onset is separated by more than the serial interval were connected by a missing generation of cases. Similarly, an imported primary case could be assumed for any outbreak or “isolated” case with no known link to an importation. Nevertheless, this method may be prone to some underestimation of the number of generations of transmission, causing $R$ to be underestimated.

Summary

Together, these criteria enable the value of $R$ after elimination to be estimated from case and outbreak data and therefore provide a tool for evaluating the status of elimination. Application of the criteria will always produce an estimate of $R < 1$. If the criteria are mistakenly applied to data from a period during which sustained transmission occurred (but was reported as a series of outbreaks because of undetected links in the chain of transmission), the estimated value of $R$ would be fractionally less than 1.

INTERNATIONAL TRAVEL

International travel statistics provide a basis for estimating the number of infections that might be imported. Each year, millions of visitors travel to Canada, the United Kingdom, and the United States, and millions of their residents travel to foreign countries (table 1). The risk of infection varies according to the level of disease control in the country from which the person arrives. For example, diseases such as mumps and rubella, for which many developing countries do not vaccinate, have a greater probability of being imported than does measles, for which vaccine programs are available worldwide. The risk of a traveler being infectious also differs for a returning resident and a foreign visitor because of their different susceptibility levels and their pattern of mixing with the foreign population. Similarly, the risk of secondary transmission is expected to be greater for residents than for visitors because of their greater contact with the population.

APPLICATION TO MEASLES EPIDEMIOLOGY

This section of the paper reviews the epidemiology of measles in Quebec, Canada; the United States; and England and Wales. The criteria presented earlier are applied to outbreak data (tables 2 and 3) to estimate the values of $R$ in each country at different time periods (table 4).
TABLE 1. Numbers (in millions) of visits for one or more nights for travelers from and to Canada, the United Kingdom, and the United States, according to area of origin, 1995*

<table>
<thead>
<tr>
<th>Area of origin</th>
<th>Canada</th>
<th>United Kingdom†</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>From</td>
<td>To</td>
<td>From</td>
</tr>
<tr>
<td>North America‡</td>
<td>15.0</td>
<td>14.5</td>
<td>3.1</td>
</tr>
<tr>
<td>Western Europe</td>
<td>1.6</td>
<td>2.0</td>
<td>33.8</td>
</tr>
<tr>
<td>Rest of the world</td>
<td>1.9</td>
<td>1.8</td>
<td>4.4</td>
</tr>
<tr>
<td>Total</td>
<td>18.5</td>
<td>18.3</td>
<td>41.3</td>
</tr>
</tbody>
</table>

† All visits (duration not specified).
‡ Includes Canada, the United States, and Mexico but excludes travel within the same country.


<table>
<thead>
<tr>
<th>Years</th>
<th>Average annual no. of cases</th>
<th>Cases imported (%)</th>
<th>No. of outbreaks with ≥5 cases</th>
<th>% of outbreaks by no. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1985–1986</td>
<td>4,552</td>
<td>2.7</td>
<td>152</td>
<td>61 26 13 0</td>
</tr>
<tr>
<td>1987–1988</td>
<td>3,526</td>
<td>2.4</td>
<td>124</td>
<td>69* 22* 9* 0.3*</td>
</tr>
<tr>
<td>1989–1991</td>
<td>18,607</td>
<td>1.0</td>
<td>754</td>
<td></td>
</tr>
<tr>
<td>1992–1994</td>
<td>1,171</td>
<td>6.1</td>
<td>52</td>
<td>73 23 4 0</td>
</tr>
<tr>
<td>1995–1997</td>
<td>318</td>
<td>16.5</td>
<td>30</td>
<td>77 20 3 0</td>
</tr>
</tbody>
</table>


TABLE 3. Annual number of measles cases and characteristics of outbreaks in England and Wales, 1995–1998

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of cases</th>
<th>No. of cases imported</th>
<th>No. of outbreaks with ≥3 cases</th>
<th>No. of outbreaks by no. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995</td>
<td>59</td>
<td>7</td>
<td>3</td>
<td>3 0 0 0 0</td>
</tr>
<tr>
<td>1996</td>
<td>115</td>
<td>11</td>
<td>12</td>
<td>7 3 2 0 0</td>
</tr>
<tr>
<td>1997</td>
<td>199</td>
<td>12</td>
<td>5</td>
<td>3 1 0 0 1</td>
</tr>
<tr>
<td>1998</td>
<td>59*</td>
<td>12</td>
<td>1</td>
<td>1 0 0 0 0</td>
</tr>
</tbody>
</table>

* Includes 23 cases with onset in 1998 that were part of outbreaks beginning in 1997.

TABLE 4. Estimates of $R^*$ based on two different criteria applied to measles data for Canada, the United States, and England and Wales, 1985–1998

<table>
<thead>
<tr>
<th>Country and year</th>
<th>Estimate of $R$ from % of cases imported</th>
<th>Estimate of $R$ from size of outbreaks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quebec, Canada</td>
<td>0.67</td>
<td>&lt;0.5†</td>
</tr>
<tr>
<td>United States</td>
<td>0.97</td>
<td>0.95</td>
</tr>
<tr>
<td>1985–1986</td>
<td>0.98</td>
<td>0.90–0.95‡</td>
</tr>
<tr>
<td>1987–1988</td>
<td>0.99</td>
<td>0.90–0.95‡</td>
</tr>
<tr>
<td>1992–1994</td>
<td>0.94</td>
<td>0.87</td>
</tr>
<tr>
<td>1995–1997</td>
<td>0.83</td>
<td>0.85</td>
</tr>
<tr>
<td>England and Wales</td>
<td>0.90</td>
<td>0.5–0.6</td>
</tr>
</tbody>
</table>

* $R$, effective reproduction number.
† All six cases were isolated.

Quebec, Canada

In Quebec, the second largest province in Canada (1997 population, 7.3 million), measles vaccination was introduced in 1970 as a single dose given at 12 months of age. Vaccine coverage in excess of 95 percent greatly reduced the incidence of measles, but epidemics continued to occur in 5- to 6-year cycles (Quebec Ministry of Health, unpublished data). In 1989, an epidemic started in Montreal and spread during a few months throughout the province of Quebec, leading to more than 11,000 reported cases (9). This situation is a clear example of sustained transmission of measles. In 1996, a large catch-up campaign provided a second dose of measles vaccine to 85 percent of school-aged children (10). As a result of this campaign, the epidemiology of measles has changed; only
six cases were reported in 1997 and 1998, none of which was linked. Two of these cases were imported, and there is no sustained transmission (Quebec Ministry of Health and Social Services, unpublished data). These data suggest that the value of $R$ for measles in Quebec is less than 0.7, and possibly much lower.

**United States**

Measles vaccine was introduced in the United States in 1963 as a single dose scheduled at age 9 months. This age was increased to 12 months in 1965 and to 15 months in 1976. In practice, many children were vaccinated later, but coverage by the time children entered school was high. The older age at vaccination resulted in a smaller proportion of vaccine failure than the Canadian 12-month schedule did; consequently, fewer US schoolchildren remained susceptible. This program may have been sufficient to maintain $R$ at less than 1. The numerous outbreaks in 1985–1986 did not reach the size of those observed in Canada (11). However, the high proportion of large outbreaks (table 2) leads to an estimate of $R = 0.95$. This example is clear evidence that the population was not far below the elimination threshold and that addition of more susceptible persons was likely to shift $R$ to above 1.

During 1989 and 1991, the number and size of US outbreaks changed dramatically (table 2) (12). The mean numbers of outbreaks (five or more epidemiologically related cases) recognized annually between 1985 and 1988 and between 1989 and 1991 were 69 and 251, respectively. The size of the outbreaks was smaller during the former period (average number of cases, 34–45; none of more than 1,000 cases) than the latter period (two outbreaks involving 2,440 and 7,514 cases). Outbreaks that previously affected predominantly school-aged children then were observed predominantly among preschoolers, and the proportion of vaccinated cases decreased from 46 percent before 1989 to 37 percent in 1989 and 19 percent in 1990. Failure to adequately vaccinate preschool children led $R$ to increase to more than 1 in some regions of the United States, opening the way to sustained transmission. Estimates of $R$ obtained under the (invalid) assumption that $R$ is less than 1 are very close to this threshold (table 4), confirming the need for caution when interpreting them.

Implementation of a two-dose schedule (13) and improvement in preschool coverage has reduced the number of cases, and the epidemiology of measles is now driven by importations. Since 1991, the Pan American Health Organization measles elimination initiative has reduced the risk of importations from the Americas, although measles remains common on all other continents (14). As a result of this initiative, the average annual number of imported cases detected in the United States decreased from 145 between 1986 and 1991 to 61 between 1992 and 1994 (15). The degree of secondary spread has also been reduced because of the steady reduction in $R$ to approximately 0.80–0.85 in 1995–1997.

**England and Wales**

A similar epidemiologic situation has been achieved in the United Kingdom following a national measles vaccination campaign in November 1994 for all children aged 5–16 years (Communicable Disease Surveillance Centre, London, United Kingdom, unpublished data). In the four years (1995–1998) following the campaign, only 432 cases of measles infection were confirmed in England and Wales, despite enhanced surveillance in which more than 15,000 clinically suspected cases were investigated in the laboratory. Many of these cases occurred in small clusters (table 3); one larger outbreak involved 150 confirmed cases in a community that refused vaccination, but there was no spread to the rest of the population. No other outbreaks exceeded 10 cases. This distribution of outbreak sizes suggests that $R$ is between 0.5 and 0.6. In all, 42 imported cases were identified, although the true number of imported infections is likely to be considerably higher given the difficulty of identifying infections in short-stay visitors. Thus, these data will lead to an overestimate of $R$. Indeed, it is likely that the total number of measles importations into the United Kingdom and the United States is similar, given the high number of European visitors to the United Kingdom (table 1). A 1995 serologic survey confirmed the low level of susceptibility in the population; from these data, the value of $R$ was estimated to be no greater than 0.7 (16). This value is intermediate between the values estimated from outbreak sizes and the proportion of cases imported and may be regarded as the most robust.

**DISCUSSION**

This paper presents a conceptual framework for evaluating the epidemiology of infectious diseases under the elimination threshold. It describes the qualitative as well as quantitative difference in the epidemiology of infection on either side of this threshold. The qualitative difference is that over this threshold, transmission continues and the number of cases becomes large if no intervention is performed; below the threshold, the number of cases is limited and transmission stops naturally. Once the population is below the threshold, any
further improvement in the population’s immunity provides only quantitative changes in the epidemiology by reducing the degree of secondary spread from imported cases. For example, if \( R \) is reduced from 0.8 to 0.5, the average number of secondary cases produced by an importation will be reduced from five to one. To eliminate infectious diseases, it is essential to maintain \( R < 1 \), but the choice of a target value for \( R \) will depend on the acceptability of a few cases and the safety margin required. The lower the value of \( R \) targeted, the greater the resources required.

Paradoxically, outbreaks should be expected to continue to occur after elimination has been achieved. Most importations of disease will produce little or no secondary transmission, but, if importations are sufficiently frequent, larger outbreaks occasionally will occur (perhaps involving 100 or more cases). If elimination is perceived as the absence of secondary indigenous transmission, such outbreaks will erroneously lead to the conclusion that a vaccination program has not achieved this objective. The occurrence of such outbreaks does not indicate that a population is above the elimination threshold: such evidence is provided only by sustained transmission in the community. Since several generations of cases can occur in populations well below the elimination threshold, any definition of elimination based on the maximum number of cases or number of generations of cases permitted in any individual outbreak is necessarily arbitrary and without epidemiologic justification. Sustained transmission should not be defined on the basis of a small number of generations of cases in a few outbreaks but rather by looking at the general epidemiology at the state or country level.

**Model**

Our model assumed homogeneity of susceptibility and mixing in the population. Heterogeneity of susceptibility will produce larger outbreaks in more susceptible pockets of the population and smaller ones in the better-protected part of the population. Large gatherings of members of the general population (such as crowds at sporting and other events) result in increased contact and hence provide an increased opportunity for transmission of infection. Importations are likely to be heterogeneous, concentrated in cities that attract tourism and international business and have large immigrant populations and universities attended by foreign students. The degree of heterogeneity can be evaluated by assessing the distribution of outbreak sizes; any large variation from that predicted by the homogeneous model suggests that marked heterogeneity is present in the population. In that situation, efforts should be made to identify the subgroup in which greater transmission occurs so that appropriate interventions can be targeted accordingly.

Our model also ignored depletion of susceptible persons, an assumption that is invalid in closed settings in which the potential for transmission of infection is increased. These settings may include pockets of unvaccinated persons (e.g., in communities that refuse vaccination) or residential institutions in which contact rates between persons are high (e.g., in universities, colleges, or military barracks). However, outbreaks in such settings usually provide little information about the potential for transmission in the general population. The degree of spread to the population outside the closed setting provides a better indicator of this potential. Classification of outbreaks by setting is therefore required.

The possible effect of outbreak control measures on reducing the size and duration of outbreaks was also ignored. Effective interventions would reduce the size of outbreaks, and failure to incorporate them would cause \( R \) to be underestimated. However, for infections with short serial intervals (e.g., measles), vaccination in response to an outbreak is often conducted too late to have any significant impact.

We have implicitly assumed that each outbreak is initiated by a single primary case. Two or more coprimary cases would on average cause a larger outbreak than a single primary case would. However, this is unlikely to be the most significant source of error in the estimates of \( R \).

These limitations of our model do not invalidate the conclusion that the degree of transmission in the population at large provides a good indication of the general level of immunity. Chains of transmission that were self-limiting with only a few cases would provide good evidence that the population is under the elimination threshold. Conversely, sustained transmission would show that the population was over the epidemic threshold and that the vaccination program targeting elimination had failed.

**Criteria**

Each of the three criteria presented for estimating \( R \) after elimination has different biases and is not equally easy to apply. It is simplest to derive \( R \) from the proportion of cases imported, but this criterion may result in overestimating the value of \( R \) because of the problem of identifying infections in visitors. Distribution of outbreak sizes is probably the most robust criterion, because the minimum outbreak size considered can be selected to suit the sensitivity of the surveillance system. The value of \( R \) can be estimated quickly by comparing the data with figures 2 and 3 or more rigorously by using standard maximum likelihood techniques.
This method will underestimate $R$ if not all cases from outbreaks are reported. Distribution of the number of generations (outbreak duration) also presents practical problems, because cases can result from overlapping generations that occur in outbreaks. Nevertheless, the number of generations can be estimated by dividing the entire length of the outbreak by the mean duration of a single generation. If a significant proportion of infections in each outbreak is not reported (e.g., because of subclinical infections), use of outbreak duration may produce less-biased estimates than use of outbreak size.

In general, for the measles data presented, the values of $R$ derived from the proportion of imported cases are higher than those derived from the distribution of outbreak sizes. The true value probably lies between the two estimates. These results suggest that Quebec, the United States, and the United Kingdom all currently represent the situation in which susceptibility to measles is beneath the epidemic threshold and sustained transmission cannot occur. Elimination of measles should be sustained provided that low levels of susceptibility are maintained by high coverage with two doses of vaccine. The same result can be achieved by adopting a high-coverage, one-dose measles vaccination schedule followed by a high-coverage measles vaccination campaign every ≤4 years for children aged 1–4 years, as has been recommended by the Pan American Health Organization (14).

**Implications for surveillance**

The occurrence of multiple chains of transmission below the epidemic threshold has important implications for outbreak control strategies and surveillance in countries aiming for elimination. For a population below the elimination threshold, intensive control measures during an outbreak are not necessary, because outbreaks will die out by themselves without intervention. As the total absence of a response to an outbreak is often politically unacceptable, public health officials should feel comfortable with less-aggressive intervention, knowing that transmission is self-limited. If no or small outbreak control measures are to be implemented, there is less need for intensive, rapid reporting of all cases.

Surveillance should be capable of detecting an (impending) failure of the elimination strategy, a failure to implement this strategy correctly, or foci of transmission in which additional measures may be needed. An active search for every isolated case provides little if any benefit, since only large clusters of cases would provide evidence of the program's ineffectiveness. Detection of all outbreaks above a certain size (e.g., five cases) is sufficient to enable $R$ to be monitored by assessing the distribution of outbreak sizes, provided that all cases in these outbreaks are reported. Surveillance should therefore emphasize linking of cases; in practice, however, it is likely that there often will be missing links between cases, even for diseases that always prompt medical consultation. Therefore, it may be reasonable to assume that cases of a rare disease occurring in temporal and geographic clusters are linked (16). When the incidence is low, specificity of surveillance becomes paramount and laboratory confirmation of cases is necessary. The surveillance required extends beyond identifying cases to adopting other methods of monitoring the susceptibility of the population, for example, measurement of vaccine coverage and serologic surveillance.

Recent developments in genotyping of organisms enhance the opportunity for studying chains of transmission (17, 18). Isolation of different strains and the failure to find any persistent strain may be used as evidence that sustained transmission has been eliminated. However, the converse is not necessarily true: repeated isolation of the same strain may indicate repeated introductions from the same external reservoir rather than sustained transmission within the population.

While this work focuses on achieving elimination through mass immunization programs, the framework can equally be applied to assessing the epidemiology of other transmissible infections. For example, more than 50 percent of hepatitis A cases in Sweden are imported (19). This finding suggests that $R$ is less than 0.5, well below the threshold for sustained endemic transmission.

**Conclusion**

In conclusion, some secondary transmission from importations will continue to occur after elimination has been achieved. As long as the susceptibility of the population remains below the epidemic threshold, however, importations cannot reestablish endemic transmission and should not be considered a threat to elimination. Rather, they provide an opportunity for monitoring the susceptibility of the population relative to this threshold through surveillance of the degree of secondary spread of infection.

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REFERENCES


APPENDIX

We modeled spread of infection and distribution of outbreak sizes arising from an importation by using a branching process (8). A further assumption was required about the distribution of the number of infectious contacts made by an infected person. In keeping with our homogeneous mixing assumption, we assumed that this quantity was Poisson distributed with a mean \( \lambda \). If this assumption is made, the outbreak size, \( S \) (including the initial importation), follows the Borel-Tanner distribution (20):

\[
\Pr(S = k) = \frac{(k - 1)! \cdot e^{-\lambda k^{k-2}}}{(k - 1)!}, \quad k = 1, 2, \ldots
\]

We also calculated the number of generations of spread, \( G \), which we call the duration of the outbreak (the imported case defines generation 0). Let \( E_k(x) \) denote the iterated exponential function (the number \( x \) to the power of \( x \) to the power of \( x \) ... \( x \) times, so that \( E_0(x) = 1, E_1(x) = x, E_2(x) = x^x \), etc.). It can be shown (21) that the cumulative distribution of the duration of outbreaks is given by

\[
\Pr(G \leq k) = e^{-\lambda E_k(e^{\lambda e^{-x}})}, \quad k = 0, 1, 2, \ldots
\]