Can a Minimum Rate of Investigation of Measleslike Illnesses Serve as a Standard for Evaluating Measles Surveillance?

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To determine whether measles case finding is sensitive, we developed a standard by which to evaluate measles surveillance. We compiled data on the incidence of measleslike illnesses (MLIs) from multiple, diverse sources and used the distribution of these values to determine the minimum level of measles case-finding activity that could be expected in a given region. Among surveillance programs in the United States, other countries in the Americas, and other World Health Organization regions, the median annual rates for rash investigations that were ruled out for measles were 4.3, 4.1, and 1.8/100,000 population, respectively. The annual rates of measles IgM testing in the United States in public laboratories and commercial laboratories were 1.6 and 9.2/100,000 population, respectively. In total, we collected data on annual MLI incidence from 180 sources. Values ranged from 0.1 to 22.6 cases of MLI per 100,000 population, and 90% of values were ≤1.0/100,000 population.

On the basis of these findings, we propose that programs attempting measles elimination consider evaluating surveillance by comparing the annual rate of suspected measles investigations against a minimum standard of 1/100,000 population.

Adequate surveillance is crucial to measles elimination efforts, to detect circulation of measles virus if it occurs. However, assessment of the adequacy of measles surveillance systems is not straightforward, because the true numbers of cases are not known. In the United States, we have used a variety of methods to evaluate measles surveillance [1]. Several of these methods would not be useful in other countries, because they depend on particular aspects of the US surveillance system or require information that is not readily available. Herein, we investigate whether another measure, analogous to the strategy used to assess the adequacy of polio surveillance in the global polio eradication effort, could be used to evaluate the adequacy of measles surveillance.

As part of its successful polio eradication effort, the Pan American Health Organization (PAHO) introduced an effective strategy to monitor the quality of case-finding activity [2–6]. In that strategy, case finding was enhanced and directed at the syndrome of acute flaccid paralysis (AFP) that included paralytic poliomyelitis but also included additional conditions, such as Guillain-Barré syndrome. When this enhanced surveillance was implemented, AFP was found to occur at a relatively stable incidence in the absence of polio itself. It was soon recognized that reports of nonpolio AFP could be expected to be ≥1/100,000 children <15 years of age annually, as long as case finding was adequate: Countries that reported at least this many cases of AFP and that effectively investigated them with laboratory testing to rule out polio were likely to truly have no circulating polio. When such countries report 0 polio cases, the report is credible because the level of investigation of patients with polio-like illness is adequate. Although the actual incidence of nonpolio AFP likely varied over time and by region, establishment of this standard of 1 AFP investigation per 100,000 children <15 years of age provided an effective management tool with which to ensure the quality of polio case finding [2–14].

For measles surveillance, the analogue to AFP would be measleslike illness (MLI): a syndrome consisting of...
a generalized maculopapular rash with fever in persons of any age. A variety of illnesses cause febrile rash syndromes similar to measles, so that even in the absence of measles, a substantial amount of diagnostic activity and investigation should occur to rule out measles and diagnose these illnesses appropriately. It would be ideal to have a standard for the incidence of MLI with which to determine whether diagnostic activity is sufficient to detect measles should it occur. However, unlike AFP, febrile rash illnesses, such as rubella or dengue fever, may be common, nonspecific, and often not severe, and their epidemiology is likely to vary substantially over time and by geography. Nevertheless, although wide variations in the incidence of MLI occur, relevant, population-based data exist relating to the incidence of MLI across many settings. By determining the distribution of values across a wide variety of settings with varied conditions, a standard can be established based on the lowest incidence of MLI that could be expected at any particular site. This standard could be used to set a minimum level of investigation that measles surveillance programs should be conducting, and it would thus not be directly affected by large variations in the incidences of MLI above that minimum.

Herein, we present data on the incidence of MLI from multiple settings with different conditions, collected by various methods. We use these data to determine the distribution of values and to propose a minimum standard incidence of MLI that could be expected in any particular site. On the basis of these data, managers of regional and national measles elimination programs can choose whether to evaluate rates of MLI investigation in their settings to ensure the adequacy of surveillance.

METHODS

Data from surveillance systems regarding number of measles investigations. Countries conducting enhanced measles control generally collect periodic data regarding numbers of suspected measles case investigations that are ruled out, or discarded, on the basis of laboratory testing. These data on number of “discards” provide information relating to the incidence of MLI in the absence of true measles. Countries in the PAHO region have been reporting these data for much of the 1990s, using standard methods and case definitions [2–6]. We evaluated data for 1997–1999 from 21 PAHO countries (excluding the United States) with a population of ≥1 million on the number of cases that were discarded by laboratory testing. Few suspected measles cases were not tested (median annual rate, 0.03/100,000 population), and they were not included in the analysis. Data for 1999 are provisional and in some instances were not available.

We also evaluated data on measles discards provided by public health authorities in 13 national or subnational programs in other regions of the World Health Organization (WHO) where measles surveillance is generally not as well developed; the population for each of the 13 reporting units was ≥1 million. A median of 0.6 suspected measles cases/100,000 population per year was not tested serologically among these sites (as much as 11.4/100,000 population for 1 country); these cases were similarly excluded from analysis. Although all programs used standardized case definitions, 11 began collecting and compiling data on discarded cases only and are still in the process of fully implementing these activities. Two programs from the European region have been collecting data on measles investigations for ≥5 years, and data from these countries may be more complete.

During 1986–1992, the Centers for Disease Control and Prevention (CDC) collected data from the states, New York City, and Washington, DC, regarding numbers of measles investigations and discards. Data were not collected during 1991, and data on the proportion of cases discarded without laboratory testing were not available. During the large measles epidemic in 1989–1991, public and clinical awareness of measles was heightened, programs were aggressive about investigating all rash illness cases that came to their attention, and ascertainment was likely to be fairly complete. Indeed, rates of measles discards during 1989–1990 were at least twice as high as rates during the years immediately before and after the epidemic. We evaluated these domestic data on measles discards for 1989–1990.

Data from laboratories regarding number of diagnostic measles tests. The volume of diagnostic measles laboratory tests can provide information on the numbers of investigations of MLI that is not subject to incomplete reporting, although such data would miss MLIs for which the clinician elected not to conduct laboratory testing. In 1994, the CDC conducted a survey of public health laboratories in the United States and collected data regarding the volume of measles IgM testing. These data would generally reflect investigations conducted by local and state health departments.

In the United States, however, most patients with MLIs present to their private providers, who would in turn generally send specimens to commercial laboratories if they wish to investigate the diagnosis of measles. As part of its responsibilities for administering the Clinical Laboratory Improvement Amendments (CLIA) program, the CDC in 1997 conducted a survey of laboratory testing services by drawing a national probability sample of 2000 CLIA-certified clinical laboratories [15]. Laboratories were sampled on the basis of type, region, and total volume of testing. Just 1 format of measles IgM assay from a single manufacturer was selected by means of this random sampling scheme, and only 1 surveyed laboratory used that particular assay. We used the results from this survey to derive an estimate of national measles IgM testing conducted in commercial laboratories.

In addition, we conducted a limited survey of commercial
Surveillance data from international settings. Figure 1a shows data on measles discards provided by PAHO for 1997–1999. The data are not presented to compare program performance, but instead to reveal patterns that can allow inference regarding rates of actual rash illness (individual sites are deliberately not identified so as not to distract from this objective). The median annual rate for these countries was 4.1 discards/100,000 population (range, 0.1–18.1 discards/100,000 population). Rates of detected nonmeasles rash illnesses were consistently higher for those countries and during those years when measles outbreaks were occurring, suggesting that when measles is visibly circulating, awareness is heightened, ascertainment is further enhanced, and more nonmeasles MLI is detected. Figure 1a includes only data regarding discards that were investigated by laboratory testing, including discards due to rubella: a median of 8% of the discards were attributable to rubella, but the proportion was as high as 73% for 1 country.

Figure 1b shows national or subnational data on measles discards from other WHO regions. The median annual rate for all sites was 1.8 discards/100,000 population (range, 0.3–12.0 discards/100,000 population). Rates of detected nonmeasles rash illness declined for both programs that have been collecting these data for longer periods as control of actual measles improved. The proportion of discards attributable to rubella is 13% for one country with good rubella control, but no data are available from the other sites regarding the proportion of discards attributable to rubella.

Surveillance data from the United States. Figure 2 shows the annual rate of measles discards, by state, for 1989–1990. The median annual value for the states was 4.3 discards/100,000 population (range, 0.6–22.6 discards/100,000 population). The portion of these MLIs due to rubella is not available.

Data from public laboratories regarding number of diagnostic measles tests. The CDC collected data from state public health laboratories in 1994 on the volume of measles IgM testing. Thirty-one states, representing 52% of the US population, provided data. Among the 31 respondents, the volume of measles
IgM testing by public laboratories in 1993 was 2091; the average annual rate of tests was 1.6/100,000 population, with a median of 1.2/100,000 population (range, 0.1–25.6/100,000 population).

**Data from commercial laboratories regarding number of diagnostic measles tests.** On the basis of a single data point from a survey on testing services at CLIA laboratories, an estimated national volume of 28,420 measles IgM tests were conducted in 1997, for a rate of 10.6 tests/100,000 population. With only 1 volume reported, however, results are not robust and confidence limits could not be calculated.

In the survey of high-volume commercial laboratories, 29 laboratories were contacted and asked to provide data regarding the volume of measles IgM tests that they had conducted during 1999. Of these laboratories, 17 did no measles IgM testing or referred measles IgM tests to reference or to public laboratories. All of the remaining 12 laboratories provided data, although in some instances they were not complete. Together, these 12 laboratories conducted 25,207 measles IgM tests during 1999. Thus, nationally, the rate of measles IgM testing by these laboratories was 9.2 tests/100,000 population. Aside from providing information with which to establish an MLI index, these data provide reassurance that there is a large volume of measles testing activity occurring in the United States.

**Validation of laboratory data as an index of MLI.** To determine whether the volume of measles IgM testing is a valid index of MLI diagnostic effort, we reviewed medical records for patients who had undergone measles IgM testing at a large HMO. Of 95 measles IgM tests conducted during 1996–1999, an indication for testing was documented in 87 records. Sixty-six (76%) of these 87 tests had been ordered by a variety of providers to evaluate patients with rash illness. The volume of measles IgM testing thus seems to provide a reasonable index of investigative activity for MLI.

**Distribution of data from all sources and sites.** In total, we collected data on the incidence of MLI from 86 international and domestic surveillance programs and from public and commercial laboratories in the United States. The values ranged from 0.1 to 22.6 cases of MLI/100,000 population/year. Approximately 90% of values were ≥1.0 case/100,000 population/year, and ∼25% of values were ≥2.0 cases/100,000 population/year.

### DISCUSSION

The AFP standard has been an extremely effective tool with which to assess the quality of polio surveillance, and it has played an important part in the success of polio eradication efforts [2–14]. Establishment of a minimum standard rate of investigation to assess the adequacy of measles surveillance, however, raises new challenges. Unlike AFP, MLIs are common and often not severe; patients are less likely to seek medical attention and practitioners less likely to report these illnesses (that had, after all, been ruled out for measles) than would be the case for AFP. Furthermore, numerous conditions can cause MLI, each with its own local epidemiology. As a result of these factors, the reported incidence of MLI is more variable than that of AFP. It would therefore be inappropriate to establish an MLI minimum standard based on any single jurisdiction. Nonetheless, population-based data exist from various settings with their variable epidemiology, spectrum of rash illnesses, health care access, diagnostic and laboratory-testing practices, case-finding systems, and reporting practices. Although each source of data reflects local circumstances and different approaches for ascertainment, by examining data from multiple sources, one can make some general observations regarding a minimal expected incidence of MLI and thereby establish a tentative minimum standard rate of investigation of MLI. This is precisely the approach that was used to establish the AFP rate that has proven so successful in ensuring the adequacy of polio surveillance [2, 7–9].

We collected data from 86 international and domestic surveillance programs and from public and commercial laboratories in the United States. The annual incidence of MLI as determined from these sources varied from 0.1 to 22.6 cases/100,000 population. About 90% of values were ≥1.0 case/100,000 population, and ∼25% of values were ≥2.0 cases/100,000 population. Another study was conducted to evaluate the incidence of MLI in an ambulatory, managed-care setting in the United States during 1995–1999; the annual rate of MLI in this study was 4.5 cases/100,000 population [16].

There are several limitations to using data on discarded measles investigations to establish an MLI standard. Age-specific data were not available to allow for the inclusion of age in the index. Also, some discarded cases reported by sites were ruled out without laboratory testing and may have included true measles, although the number of untested cases was small. A larger portion of MLI cases were due to rubella. The incidence of MLI would be slightly increased by such cases, and an MLI standard would be correspondingly inflated for programs with good measles and rubella control. On the other hand, the US data on discards represent only those cases that were reported to the CDC: Private providers and even local or state health departments may have not reported illnesses that they had ruled out for measles, so that our data regarding the rate of MLI investigations in the United States may be an underestimate.

There are also caveats to be considered in defining MLI incidence on the basis of volume of measles IgM testing. First, although some providers may choose to investigate MLI by use of increases in measles IgG titers in acute and convalescent sera, this is almost certainly an uncommon practice. A more serious limitation of these data is that measles IgM testing may be ordered without a specific intent to investigate an MLI; documentation of measles immunity is a common pre-employ-
ment and prematriculation requirement in the United States, and the volume of measles immunity screening taking place in laboratories is substantial. A high proportion of measles IgM testing could therefore be attributed to even a small proportion of anomalies in ordering practices (i.e., due to provider or clerical error or due to grouping of necessary and unnecessary serological tests as laboratory panels). We found that at 1 large HMO, measles IgM testing provided a correct measure of MLI investigation 76% of the time, but these data may not be valid for the commercial laboratories queried in our survey.

There are no objective criteria for setting surveillance standards by use of a particular distribution of data. As is the case for the AFP index and, indeed, for other quality performance indicators, the goal of an MLI standard is to serve as a management tool with which to promote quality by monitoring the performance of the surveillance program. As for all quality performance indicators, the numerical values are secondary and the powerful strategy is primary. One can assume that good and bad program performance will occasionally be misclassified by such indicators. Whereas it is important for the purposes of credibility to set standards so that misclassification is minimized, the overriding objective is to ensure that any circulation of disease is being detected.

On the basis of the distribution of reported MLI incidence from multiple sources, we propose that an annual standard of 1 investigation of MLI/100,000 total population could be used by many measles surveillance programs attempting measles elimination. Because most sites in our survey appeared to report a higher incidence of MLI, the proposed standard would serve as a specific but insensitive marker for weak surveillance performance. The quality of measles surveillance would need to be investigated for any program reporting fewer cases of MLI, though higher rates would not necessarily provide assurance that surveillance is adequate, because other rash illnesses could be circulating in those regions. As is the case for any performance indicator (and, in general, for any classification scheme), no single evaluation should be used alone to evaluate a surveillance system: If ancillary evidence exists to suggest that a surveillance program is not performing adequately, the program would need to be further evaluated regardless of its rate of MLI investigation.

Crucial to the success of this—or any—surveillance standard is the requirement that laboratory investigation be conducted for a high proportion of all MLI investigations. The WHO has suggested that laboratory testing should be conducted for ≥80% of all measles investigations [17]. We propose that only investigations in which measles is excluded by laboratory diagnosis be included in the minimum standard assessment.

A minimum standard for MLI investigations would be most useful for countries with few reported measles cases to confirm that investigations are occurring. The rate of investigations should always be considered in conjunction with the incidence of measles. A high proportion of suspected cases being confirmed as measles suggests the need for an increase in surveillance, regardless of the rate of MLI investigations. The measles surveillance system should always respond to confirmed measles cases with increased investigative effort.

Although establishment of an MLI standard raises challenges, this is, to our knowledge, among the first reports to compile data on the incidence of MLI specifically to derive an AFP-like standard for measles surveillance. National and regional program managers can review these data and determine whether this approach could be useful for their settings. We invite other programs to publish accounts of their experience with monitoring rates of investigation of suspected measles cases. As additional data accumulate from measles surveillance programs and from additional special studies, this proposed minimum standard could be reviewed and refined as necessary, and its utility for guiding evaluation of measles surveillance can be evaluated in regions attempting elimination.

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References


