Classifying Infectious Disease Outbreaks to Improve Timeliness and Efficiency of Response

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ABSTRACT

Following the intentional dissemination of *B.anthracis* through the U.S. Postal Service in 2001, use of the term "naturally occurring" to classify some infectious disease outbreaks has become more evident. However, this term is neither a scientific nor an epidemiologic classification that is helpful in describing either the source or the mode of transmission in outbreaks. In this paper, the authors provide examples of how and when the public health community has recognized potentially flawed or misleading taxonomy in the past and taken steps to improve the taxonomy's accuracy and usefulness. We also offer examples of alternative terms for classifying outbreaks since inaccurate descriptions of outbreaks could potentially lead to a flawed or incomplete set of underlying assumptions about the outbreak's causal factors. This, in turn, could lead to implementing a flawed or incomplete intervention or response strategy which could extend the duration of the outbreak, resulting in avoidable morbidity and mortality. (*Disaster Med Public Health Preparedness*. 2014;8:89–94)

Key Words: infectious disease medicine, public health, epidemiologic methods, emergency preparedness

Although concerns about the risk of biological terrorism as a source of infectious disease outbreaks were raised before the intentional dissemination in 2001 of *Bacillus anthracis* through the US Postal Service,[1–3] bioterrorism was not widely considered as a likely genesis. Even when illnesses such as plague, tularemia, botulism, and anthrax were reported, a non-nefarious zoonotic or occupational exposure was presumed to have occurred, resulting in 1 or more cases of an unusual disease. However, after the *B anthracis* dissemination, use of the term *naturally occurring* to classify some infectious disease outbreaks became more plausible.[4–11]

Initially, distinguishing an illness or outbreak as naturally occurring can be reassuring, as it suggests that the public health event was not due to an attack or other sort of deliberate or criminal activity. However, naturally occurring neither describes the source (eg, food, fomites, and people) nor the mode of transmission (eg, common source, airborne, person-to-person, and vector-borne) of the outbreak.

Although the source, mode of transmission or affected population may be unknown when an outbreak is first recognized, outbreaks that can be classified or labeled as foodborne outbreaks,[12–14] occupationally related,[15–17] or hospital associated or acquired[18–20] can help better determine the type of staff, laboratory services, countermeasures, partner organizations, and resources that likely will be needed or encountered during the investigation. Being alerted that there's a *naturally occurring* outbreak of Disease "X" may be somewhat helpful, but a more specific term could be a greater asset in planning a targeted, efficient, rapid response.

Because we cannot control or prevent many naturally occurring events such as the aurora borealis, tidal shifts, or earthquakes, characterizing an outbreak as naturally occurring could suggest that little or no ability is available to control or prevent a public health event. In fact, the opposite is usually true. The marked reduction in infectious disease mortality and the substantial increase in prevention methodologies (ie, pharmaceutical and non-pharmaceutical, pre- and postexposure countermeasures, health education risk-reduction messages, universal precaution guidelines, and other regulatory interventions), have shown that many infectious disease outbreaks can be prevented and controlled.

The reason to classify a disease or an outbreak comes from the quantitative nature of science and medicine (including public health) to classify events. The purposes of this commentary are to generate discussion and dialogue within the public health community regarding (1) the importance of reducing the likelihood for mischaracterizing infectious disease outbreaks and (2) increasing the precision with which infectious disease outbreaks are described as a standard function in public health practice. This process is done so that the public health community can ultimately develop a better framework for response. We provide examples of when the public health community has recognized flawed taxonomy and taken corrective steps. Then we conclude by offering examples of alternative terms of classifying outbreaks and a modified taxonomy to foster consideration of an improved taxonomy.

We invite readers to send the authors or the journal suggestions of conventions that describe infectious disease outbreaks in a way that is accurate in indicating the extent of the problem, and useful to public health responders in formulating a response strategy. As discussed here, each term or convention has strengths and weaknesses. Several examples may be more accurate and helpful taxonomic conventions or descriptors of outbreaks than currently exist. By better classifying infectious disease outbreaks, it is hoped that more timely, precise, efficient, and properly resourced responses can be designed and implemented.

PRECEDENT FOR CHANGING TAXONOMY IN PUBLIC HEALTH AND MEDICINE

Precedent for the public health community to change taxonomy is demonstrated in the community's evolving view of injuries. Until the latter half of the 20th century, the term *accident* was used routinely for a wide variety of injuries. However, accident connoted events beyond control, which fostered a fatalistic acceptance of morbidity and mortality.[21] Replacing *accident* with *preventable injury* created a new framework for interventions that dispensed with impressions and illusions of fatalism.[22,23]

Another example of the public health community's willingness and ability to be more precise in its taxonomy was the recognition that the term *eradication* had been misused. In the 1950s, the global effort to eradicate malaria (Global Malaria Eradication Programme) deliberately excluded most of tropical Africa until more effective and economical methods could be found to eradicate the disease in such settings.[24] Implying the hope that malaria could be eradicated by using the term *eradication* before the tools and means to actually do so were available was disheartening to the public health community. By extension, it was a disservice to the at-risk populations and the involved nongovernmental and governmental organizations as well. At the Dahlem Workshop, these terms were reviewed; *elimination* of either a disease or infection was defined in terms of a defined geographical area as a result of deliberate efforts (eg, malaria, yellow fever, yaws) and *eradication* was defined as the permanent reduction to zero of the worldwide incidence of infection (eg, smallpox, rinderpest). This distinction allowed public health communities to more clearly benchmark progress in disease intervention efforts.[25]

HISTORIC AND CONTEMPORARY CONTEXT

Exactly when naturally occurring was first introduced in relation to infectious diseases is not known, although one established international standard—the Oxford English Dictionary—contains several references. Notations from the late 16th through the 19th centuries include citations such as "A natural marke or mole vpon the skin" (1598), "The inoculated cow-pox is as much milder than the natural" (1799), "About 2,500 afterwards proved to be secure from the Natural Small-Pox" (1803), and "Nateral pox is rare, as most children have been inockilate" (1899).[26] Not surprisingly, these entries occurred before the establishment of the germ theory.

Several natural or naturally occurring concepts are valid for use in the lexicon. For example, the existence of naturally occurring resistance to antimicrobial therapy is rarely debated,[27] and the existence of natural immunologic defenses is generally agreed.[28,29] Also well accepted are the existence of natural reservoirs for microbes—especially for zoonotic diseases—and the concept of natural transmission from reservoir hosts to humans, primarily through either vector-borne transmission or transmission from animals to humans.[30,31] Similarly, the constructs of a natural history or natural course of disease or infection is commonly accepted.[32]

Similar to the risk of misusing the term eradication, the risk in using an inaccurate description such as naturally occurring when characterizing an outbreak or illness under investigation, is that it could promote a potentially flawed or incomplete set of underlying assumptions about causal factors. This, in turn, could lead to implementing a flawed or incomplete intervention or response strategy, such as assigning staff with incompatible skillsets, not identifying appropriate pre- and postexposure prophylaxes, and delaying engagement with key partners. Moreover, a response strategy predicated on faulty assumptions could extend the duration of the outbreak, resulting in avoidable morbidity and mortality, although it is difficult if not impossible to prove a negative or to quantify the extent to which inefficiency in responding to an outbreak results in increased adverse effects. Public health agencies, however, may benefit from a more useful and accurate framework, rationale, or categorization scheme to direct limited public health resources to events and outbreaks that are considered most urgent.

FRAMEWORK TO IMPROVE PRECISION AND UTILITY

The key conceptual steps in the epidemiologic investigation of known or suspected infectious disease outbreaks are to (1) identify the illness, syndrome, or outbreak through public health surveillance; (2) establish and confirm the causative agent through laboratory testing; (3) describe the outbreak's epidemiology in scientific, lay, and operational terms; (4) develop hypotheses and conduct studies to identify the source and mode of spread; (5) implement interventions that reduce morbidity and mortality and end the outbreak; and

(6) develop prevention programs to reduce the likelihood of recurrence.[33] The ultimate goal for any infectious disease is its elimination or, ideally, its eradication.

Recently, the public health community has become more proficient in rapidly identifying an infectious agent of an illness or outbreak through enhanced surveillance methodologies such as syndromic and sentinel surveillance and, increasingly, to electronic laboratory reporting. Another important enhancement in early detection of outbreaks has been the improved linkage between public health and the health care system, resulting in more perceptive clinicians reporting outbreaks to public health agencies and recognizing their role as key participants in population-based prevention and control activities. The public health community also has become more proficient in determining the causative agent through investments in laboratory methods that accelerate the identification of pathogens.

In addition, advances in laboratory methods have greatly enhanced the ability to detect related factors, such as changes in drug resistance and virulence. Moreover, the standardization and interconnectedness of laboratory systems (specifically the Laboratory Response Network) to quickly and consistently confirm the identity of causative agents have been improved.[34]

The public health community also has become more proficient in initiating large-scale emergency responses, such as occurred in the 2001 intentional dissemination of *B anthracis* through the US Postal Service, the 2003 severe acute respiratory syndrome (SARS) epidemic, and the 2009 H1N1 influenza pandemic. However, because we live in an era in which responses to such problems are more complex and visible, they involve more public and private stakeholders, planners, and responders. Subsequently, public health officials must become more proficient at describing large-scale disease outbreaks to key stakeholders and partners in terms that most accurately characterize their epidemiology, scope and severity, and prevention opportunities. Moreover, these partners and stakeholders are increasingly more diverse and may include law enforcement and other first responders, as well as elected officials, the public, media, and others.

OPTIONS FOR ALTERNATIVES TO NATURALLY OCCURRING OUTBREAKS

A Dichotomous Convention

A tempting option to enhance clarity in describing infectious disease outbreaks would be to retain a dichotomous convention and categorize infectious disease illnesses and outbreaks as either intentional or unintentional. One critical factor in the intentionality of disseminating a pathogen is its impact on the usual response to the anticipated epidemiologic pattern of the outbreak (ie, the pathogen's virulence and the outbreak's expected temporal/spatial distribution). Decisions on how, when, and where to deploy the proper number, type, and locations of staff needed for the response and factors such as the availability and use of countermeasures (eg, vaccine, antibiotics, and antivirals) will likely differ if the pathogen or outbreak is manipulated, targeted, or introduced to certain locations and populations rather than if it had a more predictable temporal trajectory and spatial distribution.

A bioterrorism event (or biocrime)—arguably the ultimate intentional event—could invalidate the traditional temporal/spatial assumptions, yet still require the rapid development and distribution of new and novel reagents to laboratories or medical countermeasures to the field. The atypical appearance of an intentionally initiated outbreak would also require the development of event-specific health communication messages for the public. These messages would be required during the response to more predictable, albeit novel, pathogens such as Middle East respiratory syndrome coronavirus (MERS-CoV), some of which could involve law enforcement and public safety, elected officials, and others who are not typically included in the investigative response to suspected infectious disease outbreaks. Thus, determining whether an outbreak was an intentional action would have important practical ramifications.

Potential and substantive weaknesses, however, are associated with the adoption of this particular dichotomous convention. First, agreement would be needed regarding what was intentional. If the action was the release or dissemination of pathogens, it would suggest that the intention is to infect other people or that a level of malevolent, malicious, or criminal motive exists in the intentional action.[35] Examples of intentional releases include the large community outbreak of *Salmonella* gastroenteritis in The Dalles, Oregon,[36] and the outbreak of *Shigella dysenteriae* associated with intentionally contaminated pastries.[37]

Many intentional actions have no malevolent intent, for example, a parent choosing to send an ill child to school or a person boarding an airplane while infected with a respiratory disease. These intentional actions may result in cases of disease or outbreaks, compounding the belief that most infections follow some intentional or voluntary action. Indeed, it is not uncommon to find examples in the public health literature of intentional actions that were normative practices at the time but led to cases of disease or outbreaks.[38] For example, in 1996, a major nationwide *Salmonella* gastroenteritis outbreak resulted from consumption of ice cream that most likely was contaminated when pasteurized premix was intentionally (albeit non-malevolently) placed and transported in tanker trailers that previously carried unpasteurized liquid eggs containing the implicated pathogen. This example demonstrates the limitation of using the terms intentional and unintentional, as the action taken was intentional but the intent was not to cause harm. Using this example, it might be argued that most, if not every, foodborne outbreak involving processed or handled food characterizes

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an intentional action. Therefore, intentional (as it relates to action vs motive) would need to be defined and clarified to assure universal understanding, acceptance, and differentiation of intentional action with malevolent intent from intentional action without malevolent intent.

A Nominal Convention

Counter to a dichotomous convention, a nominal classification scheme could be based on distinguishing outbreaks as newly emerging, well-established, or deliberately caused.[39] In this approach, the nominal notation is used to describe potential for intervention. This notation may be more precise and more useful in mounting a targeted response strategy, but is not as intuitive as sorting the outbreak dichotomously into intentionally or unintentionally initiated. This notation also is problematic in attempting to relate distinct concepts (newly emerging and well established) that are temporal descriptors and not related to causation or transmission. Unintentional, however, is not a temporal description, so these terms could be combined (eg, unintentional well established) and accurate but not necessarily exclusive or helpful.

An analogous nominal classification uses the triage model.[40] This model does not imply cause or genesis but focuses on describing severity in the hope of maximizing the use of available resources. This model classifies patients (or, for public health purposes, outbreaks) as minor (a limited response should suffice), urgent (needs attention but generally permits lower priority response without devastating results), critical (requires immediate intervention for individual or immediate environment), or catastrophic (profound consequences for harm to the individual or a large segment of the population without large, immediate, well-resourced response). Either set of nominal descriptors is arguably more accurate than *naturally occurring* and likely more helpful to decision makers in implementing the most appropriate response model. The primary advantage to the nominal approach is that more cutoff points could lead to a more precise description of the event. The primary disadvantage is that a more complex (non-intuitive) set of descriptors may make adoption more cumbersome and therefore less likely to be institutionalized.

An Ordinal Convention

Another option is to develop and institutionalize an ordinal classification system for infectious diseases. One example of an ordinal classification that describes severity and the potential for person-to-person transmission of a subset of diseases is the original categorization by the Centers for Disease Control and Prevention of biological threat agents as category A, B, or C agents.[41] Other examples of a universally accepted ordinal notation of risk are the classification of hurricanes on a scale of category 1 through category 5, tornados as 0 through 5 on the enhanced Fujita scale, and the use of 1 through 5 on the abbreviated injury scale.[42] These institutionalized conventions provide a logical gradation-of-severity index of the event and may be useful for public health officials in developing and implementing a response strategy, even if the notation itself (eg, A-C or 1-5) is not descriptive. An ordinal notation of severity may also be more universally understandable to, accepted, and properly acted on by non-public health response partners such as environmental specialists, public safety professionals, and the media.

However, the strength of the conventional classification system is also its weakness, in that it primarily focuses on severity, and not temporality, etiology, or other important epidemiologic public health intervention clues. For example, when the World Health Organization used its ordinal classification of H1N1p as a pandemic, it was interpreted by the public as being synonymous with disease severity. However, not all ordinal classifications suggest severity. An example of an ordinal convention that does not infer severity in its cutoff points is the International Statistical Classification of Disease (ICD) codes. Similar to the cutoff points that infer severity (as in threat agents and natural disasters), the codes themselves are not operationally descriptive.

A Combined Dichotomous and Nominal Classification

Finally, an alternative to choosing between a dichotomous, nominal, or ordinal convention was developed following the 2009 H1N1 influenza pandemic. This classification process attempted to capture both severity and transmissibility at different stages in the outbreak.[43] It used both a dichotomous and a nominal strategy at different stages in the outbreak, recognizing that the initial classifications of severity and transmissibility are limited by the uncertainty in early data. As the outbreak matured and new data became available, a more precise, refined assessment could occur. Also, it would allow an ordinal 5-point scale of transmissibility and a 7-point scale of clinical severity to be developed, which could help focus response resources and better describe the outbreak.

For an analogous bioterrorism or all-hazards event, the framework could be based on factors such as virulence, vulnerable populations, and the availability of countermeasures (eg, vaccination, post-exposure prophylaxis, and quarantine). Additional work would need to be conducted to determine if this approach were valid for any and all infectious diseases and not just influenza. A second consideration is that the complexity of this convention is complex and may preclude it for smaller outbreaks in which approaches to investigation and management are well understood and defined. Also, the increased complexity of this taxonomy may make its universal adoption more difficult.

CONCLUSIONS

For the purpose of operationally describing infectious disease outbreaks, we have suggested that the dichotomy of

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intentional versus unintentional offers a construct that is more accurate than the current convention of *naturally occurring*. From a public health perspective, knowing that an outbreak has been intentionally created provides useful information in selecting and implementing a sound public health response strategy. It also provides useful information to partners and principal stakeholders such as law enforcement, the media, and elected officials who will either be participating or interested in the response. However, the need to better define or classify intentionality significantly limits its adoption. A nominal approach such as the classic triage system is more descriptive, but it is also more cumbersome and potentially more difficult to institutionalize. An ordinal approach is less descriptive than either a dichotomous or a nominal model but may better describe the scope and severity of the event to public health investigators and other response partners. The ordinal convention, however, also has limitations, most notably that current examples of ordinal descriptors capture severity but no other epidemiologic indicators such as time, space, and population. These latter descriptors would assist in establishing a more efficient public health emergency response. Finally, a combination of conventions that concurrently highlights transmissibility and severity appears to be accurate and potentially useful if (1) additional epidemiologic indicators could be added and (2) it could be labeled in operational terms that public health officials can use to accurately and succinctly initiate a rapid, comprehensive response strategy and tactics.

This commentary is intended to be more than an academic exercise. We are interested in identifying an improved and more accurate public health terminology that public health agencies can use to develop and conduct the most rapid, efficient, and effective response strategies to interrupt infectious disease outbreaks, especially in this era of limited resources. Although it is likely impossible to prevent a new or novel illness or outbreak the first time it appears (as with SARS, Pontiac fever, and AIDS), we believe that the myriad prevention strategies employed in our national disease control and elimination programs have contributed to the reduction in the number of, and sequelae from, many if not most infectious disease outbreaks. We also think that some temporally or spatially predictable outbreaks such as seasonal influenza cannot be completely prevented, although enhanced utilization of well-established medical and nonmedical countermeasures could drastically reduce their morbidity and mortality.

In reviewing the limitations of using the term naturally occurring to categorize infectious disease outbreaks, we believe that a new convention could be more accurate or helpful for public health agencies that must respond to infectious disease outbreaks or to the public. However, establishing an alternative, improved taxonomy poses several challenges. We hope that readers will send their suggestions for enhancing clarity and utility in classifying infectious disease outbreaks so that response strategies can be more efficiently developed and implemented than at present.

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Disclaimer

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