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If Syndromic Surveillance Is the Answer, What Is the Question?

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THE EVENTS OF FALL 2001, particularly the mailing of anthrax spores to public officials and the consequent anthrax cases, have had a dramatic and immediate effect on the perception of public health in the United States on the part of policy makers, government officials, and the general public. A public health infrastructure that has generally been undervalued and underfunded for several decades has seen a sudden infusion of substantial federal funds appropriated by the U.S. Congress and distributed to state and local health departments by the U.S. Centers for Disease Control and Prevention (CDC). This infusion of federal funds comes just as most localities and states are facing mounting budget deficits and are being forced to reduce spending across the board, including spending on important health care delivery and public health programs. As a result, these new federal funds and the programs they support are having a disproportionate impact on the priorities and activities of local and state health departments.

Those responsible for appropriating and disbursing these federal funds have almost invariably referred to the need to strengthen public health in general and to the desirability of improving our ability to detect and respond appropriately to both manmade and naturally occurring infectious disease threats. However, it seems inarguable that the impetus behind this federal largesse is to improve preparedness for possible future bioterrorist events, which some policy makers and technical experts with access to classified information believe are inevitable. Given the decades of underfunding of public health that preceded the events of Fall 2001, it is difficult to envision comparable levels of funding being made available for the sole purpose of enhancing our ability to detect, respond to, and study naturally occurring infectious diseases, even under the recently popular rubric of "emerging and re-emerging" infections.

Among the activities being funded as a part of the efforts to improve our nation's capacity to detect and respond rapidly to new infectious disease threats is *syndromic surveillance*. Syndromic surveillance is generally meant to refer to the monitoring of the frequency (e.g., the number or rate of episodes) of illnesses with a specified set of clinical features (e.g., fever and respiratory complaints, vesicular skin rashes, diarrhea, etc.) in a given population (e.g., members of a health maintenance organization, residents of a given geographic region, etc.), without regard to the specific diagnoses, if any, that are assigned to them by clinicians. Because many of the infectious agents considered likely to be used in a bioterrorist attack (e.g., smallpox, plague, anthrax, tularemia, and brucellosis, among others) initially produce nonspecific clinical manifestations (e.g., fever, malaise, cough, fatigue, anorexia, etc.), and because even the best-prepared clinicians may not suspect one of these illnesses in the absence of more specific findings, it seems plausible that careful monitoring of a syndrome like febrile respiratory illness can provide to public health officials the earliest evidence of such an attack. Earlier detection of a bioterrorist event would then enable more rapid targeting and implementation of effective control measures, including vaccination, chemoprophylaxis, or quarantine, and lead to a consequent reduction in morbidity and mortality.

Various approaches are being used to amass the data needed to measure the number or rate of such illnesses in a population, including enhanced passive reporting of illnesses seen in health care settings (e.g., hospitals, emergency departments, and outpatient clinics); active case finding in similar settings; monitoring of 911 calls; and making use of data normally being entered into computerized data bases by health care providers such as health maintenance organizations for billing and other purposes. Attempts are even being made to monitor illnesses in the community irrespective of whether the ill individuals seek medical care by examining sales of over-the-counter medications and other items.

While some of these approaches are labor intensive,

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expensive to maintain, and therefore questionable in terms of sustainability (e.g., active case finding), others rely primarily on preexisting data collected for other reasons and therefore do not require that substantial resources be devoted to data collection. What all of these approaches have in common is a primary focus on detecting time/space clustering of illnesses—that is, a higher than expected number or rate of events in comparison to some background number or rate.

The possibility of earlier detection of and more rapid response to a bioterrorist event has tremendous intuitive appeal and is probably adequate justification for funding syndromic surveillance in the minds of decision makers, the general public, and clinicians. However, many public health officials and epidemiologists have posited additional benefits that may be provided by syndromic surveillance, even if another bioterrorist event never occurs in the U.S. or if, for the reasons described below, syndromic surveillance is unable to detect such an event early enough to reduce morbidity and mortality compared to that which would have occurred in the absence of syndromic surveillance. These other benefits are said to include: more rapid characterization of the population potentially at risk following a bioterrorist event and more efficient targeting of prevention/control activities; an increase in knowledge concerning naturally occurring infectious diseases; and a general strengthening of the public health infrastructure at the local and state levels and its ability to deal with other diseases of public health significance.

Thus, the argument is made that even if syndromic surveillance is unable to meet the promise of earlier detection of a bioterrorist attack, either because such an attack never occurs in an area with syndromic surveillance in place or because syndromic surveillance proves incapable of speeding detection and response in a real world setting, it is still a worthwhile expenditure of scarce public health resources. I believe, however, that the assumptions underlying all of the arguments put forward in support of syndromic surveillance need to be held up to careful scrutiny before substantial resources are invested in this enterprise, either as a public health tool or as a research endeavor.

CHALLENGES CONFRONTING SYNDROMIC SURVEILLANCE

Demonstrating that syndromic surveillance reduces morbidity and/or mortality following a bioterrorist event

Given that funding for syndromic surveillance clearly emanates from a desire to be able to detect and respond more promptly to a future bioterrorist event than would otherwise be possible, a key question is whether, in the real world, even an optimally functioning syndromic system is likely to be able to provide more rapid detection of and response to such an event, leading to a reduction in morbidity and/or mortality compared with what would have occurred in the absence of such a system. If no bioterrorist events occur, or if they occur only in areas without syndromic surveillance in place, the system will remain untested with regard to its primary purpose. Even if a future bioterrorist attack occurs in an area with syndromic surveillance in place, and we are able to determine how quickly the event was detected and how much morbidity/mortality occurred, we will not know with any certainty what would have happened in the absence of syndromic surveillance. Thus, unless multiple, similar, and simultaneous bioterrorist attacks occur in areas with and without such surveillance in place, we will almost certainly never be able to demonstrate in a scientifically rigorous way that syndromic surveillance succeeded in meeting this primary objective (i.e., by showing that detection occurred earlier and morbidity/mortality was lower in areas with such surveillance systems than in areas without syndromic surveillance).

Although it may never be possible to demonstrate in a rigorous way that syndromic surveillance can detect bioterrorist events more rapidly than they would otherwise be detected, it is possible to assess the likely sensitivity and specificity of such systems in detecting clusters of naturally occurring illnesses, such as febrile respiratory illnesses. A number of groups have reported on the sensitivity and specificity of syndromic surveillance systems in detecting actual or simulated outbreaks of febrile respiratory illness.[1–3] For example, using computerized historical data, one group of investigators has recently reported that algorithms they have developed can detect clusters of febrile respiratory illness among members of a health plan.[2] The results of such studies suggest that if a bioterrorist attack causing febrile respiratory illness were to occur in a community, ongoing surveillance using computerized patient encounter data would detect the event in a timely fashion.

The results reported in such studies, however, are neither surprising nor necessarily evidence that systems of this kind would provide earlier detection of and reduced morbidity/mortality from such events. The results are not surprising in that they show that a team of individuals with substantial expertise in epidemiologic and biostatistical methods and access to appropriate data sources, software, and computer hardware can detect clusters of health events when they occur. The results are not necessarily reassuring in terms of earlier detection and response to a bioterrorist event, because they do not address some key practical issues.

Types of bioterrorist events that syndromic surveillance is likely to detect

Suppose that such a system is prospectively collecting data concerning febrile respiratory illnesses in a popula-

tion and, as would be necessary for the most rapid detection of a bioterrorist event, the data are being analyzed and reports to the health department are being generated daily. Further suppose that the relevant local/state health department has all of the resources needed to conduct any appropriate follow up if and when a cluster of illnesses is identified. Had such a system been in place in Florida or Maryland or Connecticut in the Fall of 2001, would it have detected any of the anthrax cases caused by the bioterrorist attack that occurred then? Perhaps, but would the system have detected an increase in the number or rate of cases of febrile respiratory illness? Probably not, because the number of cases in any one geographic area was very small (one or two). Thus, such a system can only be expected to detect bioterrorist events of a given type/size.

Response to apparent increases in illnesses signaled by syndromic surveillance

For bioterrorist events affecting more than a small number of individuals in a given geographic region, the likelihood and speed of detection will depend on what (seasonally adjusted) numbers or rates of cases are used to signal a possible cluster of cases. As has been well shown in studies examining the use of threshold rates to signal the arrival of epidemic meningitis in sub-Saharan Africa,[4–6] and as has been acknowledged in work examining ways to optimize detection of outbreaks, increases in the sensitivity of epidemic detection will come at the cost of decreases in specificity and vice versa.[2–4] Perhaps more important, the predictive value of a positive (the proportion of the time that any given threshold level is crossed that a bioterrorist event has occurred in that population) will range from zero to extraordinarily low, because most communities do not experience any bioterrorist attacks in a given time period. Thus, whatever numbers or rates of cases are used to signal a possible bioterrorist event, all or virtually all of the instances in which an excess is noted will represent false positives/false alarms.

What will the health department do when a daily report generated by the system suggests that a cluster or increase in the number/rate of cases has occurred? How will the health department determine whether the cluster is a chance event, the result of a naturally occurring disease, or the result of a bioterrorist attack? They could wait a day or two (or more) to see if the number/rate of cases continues to be too high, compared to what is expected for that population at that time of year. However, a continuing (or increasing) high number/rate of cases can only reduce the probability that the cluster is a chance event, not rule out the possibility entirely. More important, such information cannot help in determining whether the illness is naturally occurring or bioterrorist in origin. Furthermore, delaying action for a day or two to observe what happens clearly reduces the timeliness of any response and makes it less likely that the system will result in earlier detection and reduced morbidity/mortality than would otherwise occur. For example, one study examining the potential costs of a bioterrorist attack and the savings that might accrue from earlier detection found that very little in the way of a reduction in the number of deaths caused by a bioterrorist attack (with an aerosol of anthrax or tularemia) could be achieved more than four or five days after exposure to the aerosol.[8]

Whenever a decision is made to conduct some form of follow-up investigation of an observed cluster, what will that follow-up investigation entail and how quickly can it be done? Will it be sufficient to talk with the physicians of the ill individuals and examine existing medical records? Or will it be necessary to obtain additional tests (e.g., chest x-rays) and specimens (e.g., blood, serum, nasopharyngeal swabs, sputum cultures, etc.), most of which are unlikely to have been obtained during the routine clinical care of outpatients with a febrile respiratory illness? Without a firm etiologic diagnosis in hand, it is difficult to envision a health department taking any substantive action, such as distributing prophylactic antimicrobial agents, vaccination, imposing quarantine, or even issuing an alert to the public, based solely on an increased number of clinical illnesses.

But if the probability that any given cluster is the result of a bioterrorist attack is extremely low, how often and under what circumstances will it be deemed reasonable to obtain additional tests and specimens? Who will collect these specimens, and who will pay for the testing? How quickly can they be processed and results be obtained? Are these "clinical" specimens, being obtained and tested as a part of the routine care of the patient; "public health specimens," being obtained as part of an outbreak investigation; or "research" specimens, for which approval from an institutional review board and informed consent from the patient will be required? Thus, proving that daily monitoring of syndromes such as febrile respiratory illness can, given predetermined statistical parameters, detect clusters of cases does not prove that such a system can, when done prospectively in the real world, produce more rapid detection of and, more important, more rapid response to a bioterrorist event.

Plausibility that syndromic surveillance can yield more timely identification of the population at risk in a bioterrorist event

If a bioterrorist event does occur, can a preexisting syndromic surveillance system in the affected area help define in a more timely manner the affected or at-risk population in need of preventive measures, even if the system did not yield earlier detection of the event itself? It seems quite plausible that this is the case, and I suspect

that this may be the single strongest argument in favor of having such systems. However, it should be remembered that in response to the events of September 11, 2001, federal, state, and local public health agencies were able to put post-event (so called "drop-in") surveillance for adverse health outcomes in place in New York City and elsewhere very rapidly.[9] Given the heightened state of alert and the additional resources being made available in most jurisdictions and public health agencies over the past year, it seems quite likely that a response at least as rapid could and would follow the first confirmed case in an area of any illness caused by an infectious agent considered a plausible bioterrorist weapon. Thus, the window for improving on what is likely to happen in the absence of syndromic surveillance is very narrow. While the costs of implementing such "drop-in" surveillance systems are quite large, they are likely to be incurred very infrequently and almost certainly are less than the costs of implementing and maintaining ongoing syndromic surveillance systems in multiple geographic regions.

Likelihood that syndromic surveillance will produce useful information about naturally occurring infectious diseases

Will syndromic surveillance produce new and potentially useful information about naturally occurring infectious diseases, making it a worthwhile investment even if a bioterrorist event never occurs or cannot be detected significantly earlier? Perhaps, but it is worth examining this suggestion in more detail. In the case of surveillance for febrile respiratory illness, for example, what new and important information can be learned in the absence of biological specimens from the affected individuals or associated analytic epidemiologic studies of risk factors? Will the available information be limited to the descriptive epidemiologic features of febrile respiratory illnesses of unknown etiology? How important and useful would such results be? Could such a study compete for funding through traditional channels of supporting investigator-initiated research?

If biological specimens from affected individuals are to be collected and tested, the question of whether these are being collected for clinical, public health, or research purposes again arises. Furthermore, copious well-designed studies of acute respiratory infections have been conducted in the U.S. and elsewhere over the past 50+ years and have produced mountains of data concerning the etiology of and risk factors for such infections. Even if appropriately timed and properly collected specimens can be obtained from a high proportion of individuals with febrile respiratory illnesses (most of whom are not ill enough to be hospitalized or even be given outpatient antimicrobial therapy), are there new diagnostic techniques or new hypotheses to test that make such labor-intensive and expensive efforts worthwhile? If not, the likelihood that we will make significant advances in our understanding of febrile respiratory illnesses and their causes seems very low, although occasional naturally occurring outbreaks of illness caused by influenza, parainfluenza, mycoplasma, and Legionella, among other known etiologic agents causing febrile respiratory illness, will be detected.

While it might seem inarguable that there is a benefit to detecting more such naturally occurring outbreaks, that benefit will be limited by the ability of the public health and medical care systems to respond, offer treatment or prevention, or increase knowledge about the disease in question. It is worth bearing in mind that public health departments already engage in a form of triage that, of necessity, leaves many if not most suspected outbreaks uninvestigated.

Circumstances under which syndromic surveillance is likely to strengthen local and state health departments

Finally, there is the question of whether establishing syndromic surveillance systems strengthens public health departments at a time when local and state public health departments badly need strengthening and the resources for doing so are scarce. The optimal approach to using the establishment of syndromic surveillance to strengthen the state and local public health infrastructure would be permanently to increase state and local funding to hire and equip well-trained public health professionals (e.g., epidemiologists, biostatisticians, programmers, etc.) working in these agencies to establish, conduct, and analyze the results of the surveillance. Such well-trained and well-equipped individuals would then be available to conduct or assist with other high-priority public health functions. However, with most cities, counties, and states facing budget deficits, it is hiring freezes, elimination of unfilled positions, and reductions in staffing that are the order of the day, not the hiring of new staff into locally funded permanent positions.

An alternative approach is to use federal funds being distributed to the states to hire such individuals to work in the local and state health departments and establish syndromic surveillance, but allow them to assist with other functions as well. While some states may be taking this approach, it can be a protracted process under the best of circumstances. Even in states not worried about whether such federal funds will continue to be available and willing to hire new staff using such funds, the procedures for posting and filling positions can take months, and, more important, it may not be possible to find, hire, and retain epidemiologists, biostatisticians, and programmers with the relevant expertise, given competing demands for such individuals and the comparatively low salary levels in most health departments. (Even if outside, federal funds are used to hire such individuals, for

reasons of equity they generally cannot be paid salaries higher than those paid to other health department employees.) And finally, it may not be deemed advisable (or even legal) to have such employees, hired with categorical federal funds, performing or assisting with other health department functions.

Because of these problems and a perceived need to develop and test such syndromic surveillance systems expeditiously, the resources specifically targeted at establishing and testing such systems have, to date, gone primarily to academic institutions and other research organizations. While state and local health departments are key partners in some (but not all) of these efforts, the capacity to collect and analyze the relevant data remains largely external to the health departments. (For health departments without academic partners, for-profit corporations are beginning to market their services in collecting and providing syndromic surveillance data, in a manner even less likely to build capacity in the health departments themselves.) A substantial expansion in collaboration between academic institutions and health departments in both research and teaching is, without doubt, highly desirable and mutually rewarding, but substantial improvements in the local and state public health infrastructure ultimately require that additional well-trained and well-equipped public health professionals be hired and retained by these agencies.

CONCLUSIONS AND RECOMMENDATIONS

While all the arguments in favor of establishing syndromic surveillance are, on the surface, reasonable and attractive, I believe it is necessary for funders and decision makers to examine these arguments and the assumptions on which they rest in more detail. It may well be that syndromic surveillance ends up being a worthwhile investment of scarce public health resources, but I believe that case has yet to be made. With luck, the ability of such systems to provide early detection and/or improved response to a bioterrorist event will remain untested. Those calling for the establishment or continued funding of syndromic surveillance systems should be expected to spell out in far greater detail than they have thus far how such expenditures of scarce resources will enhance the readiness of public health systems not simply to detect clusters of illnesses, but to respond appropriately when they are detected, taking into account "real world" constraints.

If part of the justification for establishing such systems relies on their usefulness in conducting studies of naturally occurring infectious diseases, then proponents should be expected to provide specific plans concerning collection and testing of laboratory specimens, hypotheses that can and will be tested in such studies, and what is likely to be learned that cannot be learned equally well from existing systems for monitoring influenza, influenza-like illnesses, or other conditions. Finally, if those advocating for syndromic surveillance systems want to make a convincing case that such systems will strengthen local and state public health agencies, they need to assure that the resources invested produce real and sustainable increases in the intrinsic ability of such agencies to conduct vital public health functions.

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