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THE ROLE OF EPIDEMIOLOGY IN UNUSUAL/SUSPICIOUS OUTBREAKS OF DISEASE

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Detecting and investigating infectious disease outbreaks are major day-to-day public health activities, involving a coordinated epidemiologic and laboratory effort. The epidemiologic studies provide clues to focus and direct the laboratory effort, and the laboratory studies provide evidence to confirm (or refute) the epidemiologic hypotheses. The investigative approach would be similar whether the outbreak occurred naturally or was the result of an intentional or unintentional biological weapon release.

Overview of epidemiologic methods

Fundamental to public health prevention programs is the ability to identify outbreaks in a timely manner. An outbreak is the occurrence of disease in greater than expected numbers. Public health authorities may learn of an outbreak as the result of a surveillance (disease monitoring) system. Surveillance systems are based on a variety of strategies such as mandatory or voluntary reporting of specific diseases by microbiologic laboratories, private physicians, or hospitals. However, particularly in the case of an emerging disease, the first indication of a problem is often spontaneous reports by physicians, patients, the news media, and other unstructured sources.

When a possible outbreak is identified, the epidemiologist first confirms that a disease definable on clinical or laboratory grounds has occurred. Then the outbreak is described in terms of who (patient characteristics such as gender, age and ethnicity), where (geographic distribution), and when (time relationship of cases). Diseases do not strike randomly in a population, and this simple outbreak description is a powerful tool in determining who is at risk for the disease and where to focus the epidemiologic effort.

Determining the why and how of the outbreak is more difficult and usually involves a coordinated epidemiologic and laboratory effort. The analytic study phase of the investigation may involve various approaches. A survey may be necessary to determine the magnitude and distribution of an outbreak. A case-control study may be necessary to define risk factors for acquiring the disease. In a case-control study, affected persons are compared with unaffected persons on any number of potentially significant variables (such as diet, travel, and animal exposure) during a specific period. In complex studies, many case-control studies may be necessary as additional information becomes available. Less commonly, a cohort study may be implemented to evaluate outcomes in a group of persons who had a particular exposure (such as to Agent Orange) or were subject to some intervention measure such as anthrax vaccination or treatment with antibiotics.

Microbiology laboratory support is essential to epidemiologic investigations of infectious diseases. The laboratory may be called upon to identify the agent if the cause of the disease is unknown, to identify infected patients by testing clinical specimens or immunologic studies, to determine drug susceptibility of the organism, and to test potential vehicles of infection or reservoir hosts for the organism. Another important function is to subtype or identify features of the infectious organism that can be used to differentiate the outbreak strains of the same organism. This permits the origins of the outbreak to be traced with a higher degree of certainty, particularly in outbreaks due to frequently encountered pathogens such as *Salmonella* organisms in food-borne diseases.

Other specialists may be needed in the course of an outbreak investigation. For example, mammalogists, entomologists and veterinarians are frequently needed in diseases maintained in animal populations or transmitted by insects. Engineers may be called to evaluate water and sewer systems, inspect food processing machinery, or evaluate ventilation systems. Meteorologic information may be critical in explaining the timing of an outbreak or airborne spread of a microbe.

When the investigation has been completed, an outbreak report documenting the essential aspects of the investigation is issued. The disease definition and the investigation's objectives, methods, and data sources must be clearly stated. Results are normally presented with tables and figures that allow the reader to independently determine the reliability of the conclusions by reviewing the raw data. Statistical inferences are presented in terms of probability or odds that an event could have happened by chance alone, with a confidence interval range. Potential study biases and data voids should be identified. Epidemiologic analyses provide circumstantial evidence for the study hypotheses. Physical evidence is provided by the laboratory and other supporting studies. The report should conclude with implications of the study observations and recommendations.

Epidemiologic assessment of biological weapon releases

The principles of epidemiologic investigation are the same for a biological weapon release as for an outbreak that occurs naturally. Differences would relate to other needs such as political considerations, fulfilling treaty compliance terms, or legal requirements for evidence collection and custody.

Detecting a possible biological weapon incident, whether intentional or accidental, would present a substantial challenge. The efficiency of infectious disease surveillance systems varies widely throughout the world. No country has a perfect system for rapidly detecting emerging disease problems, and many have minimally effective surveillance at best. Even with acceptable surveillance, the intentional small-scale use of common pathogens such as *Salmonella* organisms to contaminate restaurant food, for example, could easily go undetected, lost in a background of similar naturally occurring incidents.

A country's constitution and political organization may have a significant impact on surveillance and epidemiologic investigations. In the United States, for example, the State epidemiologists, in consultation with the Centers for Disease Control and Prevention (CDC), determine which diseases are reportable on a national basis. The State epidemiologists also have great influence over epidemiologic investigations conducted within their State. Federal epidemiologists, in general, may investigate an outbreak within a State only with the concurrence of the State epidemiologist. In turn, the ultimate authority for epidemiologic investigations within a State may lie with local or country officials, with the State health department acting as a consultant. Similar situations exist in other countries. How to accommodate decentralized public health authority and responsibility will be an important consideration in developing an international compliance protocol.

Even in the absence of an effective national surveillance system, small outbreaks of unusual or highly lethal infections are surprisingly likely to be detected through informal channels such as the Internet and press reports. Despite governmental efforts to first suppress information and then provide misinformation, rumors of the Sverdlovsk anthrax incident circulated widely within weeks, followed by press reports within six months of its occurrence. Recent epidemics of *Ebola* and *Lassa* viruses provide further examples of disease outbreaks that quickly came to international attention through press accounts and informal requests for assistance.

Ways to improve international surveillance are being actively discussed. For example, a recent Trans-Atlantic Alliance Agreement between the United States and the European Union calls for a global communicable-disease network, and the United States and Japan have agreed to collaborate on improving global efforts to control emerging diseases. Translation of such agreements into working systems awaits discussions among relevant subject matter experts and allocation of appropriate resources.

For purposes of monitoring a nation's compliance with a biological weapons control treaty, open communications and wholehearted cooperation with investigations of suspicious incidents are more important than the format or quality of the country's public health surveillance system. Countries that choose to develop biological weapons contrary to a treaty cannot be depended on to voluntarily disclose information about related disease incidents, even if their surveillance will be needed to monitor the wilfully non-compliant countries.

A balance needs to be struck between confidence building on arms control measures and intrusiveness in nation's public health programs. Perhaps having an international observer participate in suspect outbreak investigations would suffice in almost all cases. In any event, agreement must be reached by treaty signatories on what constitutes a suspicious

incident, recognizing that almost all such incidents will be natural disease outbreaks. Developing an index-of-suspicion scale might be useful in designating outbreaks warranting an international evaluation. For example, on a scale of one (not needing investigation) to ten (must be investigated), a small outbreak of inhalation anthrax might be rated as a ten and a major urban salmonellosis epidemic rated a two.

Minimal standards for an epidemiologic investigation and acceptable laboratory test methodology are other areas in which consensus must be reached. CDC's epidemiologic approach to infectious disease outbreaks has evolved over the last 50 years and now has widespread acceptance and use throughout the world. There are currently sixteen international field epidemiologic training programs around the world that apply CDC's investigative methods, and more are in development. As a result of these efforts, a pool of persons, who are both skilled in CDC's investigative methods and have an extensive infectious diseases background, is already available to assist in outbreak investigations. Laboratory support should be provided by facilities with recognized expertise and the resources to apply cutting-edge science to specimen evaluation. Collection, identification, and custody procedures must be developed to preclude questions of contamination or misidentification. Provision for split and referee samples should be included in the standard procedures. Peer review of laboratory findings should be routine.

The goal of each investigation should be to determine why the outbreak occurred and how future occurrences can be prevented. Reaching this goal will require commitments of time and adequate resources. Although a working hypothesis about the origins of an outbreak may be developed in a relatively short time, testing the hypothesis will often involve intense effort for many weeks to months. How these activities will be supported on a long-term basis needs to be considered.

Investigations should commence as quickly as feasible following detection of a suspect outbreak. Timeliness of an epidemiologic investigation is directly correlated with the quality of results. Recall of events tends to fade rapidly or become confused with the passage of time. In addition, appropriate environmental and clinical specimens are more likely to be available.

Epidemiology should play a key role in monitoring compliance with a legally binding protocol to the Biological Weapons Convention. The value of epidemiology in the understanding of naturally occurring infectious diseases is without question. Similar success would be expected in the investigation of potential biological weapon incidents if adequately supported and free of political interference.
