

Investigating Disease Outbreaks under a Protocol to the Biological and Toxin Weapons Convention

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The Biological and Toxin Weapons Convention prohibits the development, production, and stockpiling of biological weapons agents or delivery devices for anything other than peaceful purposes. A protocol currently in the final stages of negotiation adds verification measures to the convention. One of these measures will be international investigation of disease outbreaks that suggest a violation of the convention, i.e., outbreaks that may be caused by use of biological weapons or release of harmful agents from a facility conducting prohibited work. Adding verification measures to the current Biological and Toxin Weapons Convention will affect the international public health and epidemiology communities; therefore, active involvement of these communities in planning the implementation details of the protocol will be important.

The Biological and Toxin Weapons Convention (1) prohibits the development, production, stockpiling, or transfer of biological weapons agents (microbial pathogens and toxins) for other than peaceful purposes and any devices used to deliver these agents.¹ The convention was the first treaty to outlaw the development and possession of an entire category of weapons, and the first to outlaw any weapon of mass destruction. There are now 143 states parties to the convention and an additional 18 signatories. Even though the convention's renunciation of biological and toxin weapons was categorical, it was not accompanied by effective provisions for verification. Article VI of the convention provides that states parties that suspect another state party of noncompliance may submit a complaint to the U.N. Security Council, and all states parties are obliged to cooperate fully with any investigation that the security council may initiate. However, this mechanism has proved inadequate. Despite several allegations of noncompliance in the 25 years the treaty has been in force, Article VI has never been invoked,

probably in recognition of the intensely political nature of security council decisions, and the crippling effect of the veto power of the five permanent members (2,3).

Recent information about the covert biological weapons programs of the former Soviet Union (4) and Iraq (5) gave added momentum to verification efforts begun in 1991. A draft text for a protocol to the Biological and Toxin Weapons Convention is now in the final stages of development and could be opened for signature and ratification within a year. One of the provisions of this >200-page protocol will be a mechanism for investigating certain outbreaks of disease to resolve suspicions about compliance with the convention (6). There are several reasons for having such a mechanism (7). An outbreak of disease might be the result of biological attack on troops, civilians, crop plants, or domestic animals. Alternatively, an outbreak could be the result of accidental escape of harmful agents from a secret biological weapons facility. A mechanism for the prompt investigation of such outbreaks by the international community would address and resolve such concerns; it would also deter the use of unsubstantiated accusations (e.g., the 1952 allegation of U.S. propaganda use of biological

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¹Although the Biological and Toxin Weapons Convention does not explicitly prohibit the *use* of biological weapons, it does so implicitly because any use presupposes prior production and stockpiling.

agents in Korea and Manchuria [8,9]) and would reduce the credibility of fraudulent investigations controlled by the accuser. Finally, the political costs of being identified as a biological aggressor could deter covert biological weapons programs (7,10).

What Outbreaks Will Be Investigated?

Thousands of outbreaks of disease occur annually among humans, domestic animals, crop plants, and wild animals and plants. The only outbreaks relevant to the weapons convention and its verification protocol are "suspicious" outbreaks, which have features suggesting an unnatural cause. The draft protocol calls for requests to investigate outbreaks to include "detailed evidence, and other information, and analysis that such an outbreak(s) of disease is not naturally occurring and is directly related to activities prohibited by the Convention" (6). Thus, very few outbreaks would likely become issues of treaty compliance.

An outbreak might be suspicious because epidemiologic features suggest an unnatural origin. For example, in the 1979 anthrax outbreak in Sverdlovsk, former Soviet Union, the distribution of both human and animal cases in a narrow corridor downwind from a military microbiology facility was a strong indication of unnatural origin (11,12). Also, the etiologic agent may differ from agents naturally found in the environment, as would be the case if the agent were genetically engineered; in such an event, the unusual phenotype of the agent would signal something anomalous. Detailed molecular study, including DNA sequencing, should reveal the recombinant nature of the organism.

Even in the absence of genetic engineering, agents used as biological weapons may differ in recognizable ways from those causing natural cases of the same disease. This would be the case if the weapons agent had been maintained in laboratory culture for some time before use. Because of natural selection and genetic drift, each population of an organism continually diverges genetically from others of the same organism. It is thus possible in principle (and in practice for many agents) to determine the geographic origin of an outbreak with the tools of molecular epidemiology, by determining to which local population its etiologic agent belongs. An outbreak caused by a strain last seen many years ago could be suspicious (7,10).

Other features of the agent can also be suspicious. For instance, in the Sverdlovsk outbreak, retrospective molecular analysis of retained pathology samples showed that patients appeared to have been simultaneously infected with several strains of the anthrax agent (13); multiple infections are not normally encountered in natural outbreaks.

In addition to unusual epidemiologic features, devices used to disseminate the agent and intelligence information can help identify a suspicious outbreak. For example, the 1993 outbreak of intestinal illness among the insurgent Karen of Burma (Myanmar) (14-16) was suspicious largely because a number of putative delivery devices (balloons attached to meteorologic radiosondes and parachutes) were recovered.

Labeling an outbreak suspicious reflects a judgment that the evidence suggests unnatural causes. Different analysts can come to different conclusions, and political or ideological factors can affect the judgment. Thus, compiling a list of features that would automatically render an outbreak suspicious is not possible. Probably, most or all suspicious outbreaks will turn out to be natural occurrences.

Types of Suspicious Outbreaks

Suspicious outbreaks can be grouped into four main categories, depending on the nature of the suspicions they provoke. They may be thought to be the result of covert biological attack by another nation, criminal or terrorist attack, covert attack by a nation on a subnational group within its borders, or escape of a biological agent from a facility developing prohibited weapons.

If a nation suspects it has been biologically attacked by another nation, it would most likely be the one to request an investigation and could be expected to cooperate fully. However, despite the cooperative attitude of the host nation, its vested interest in the outcome of the investigation requires the investigating team to be alert to the possibility that information provided by official sources may be biased, incomplete, or even fraudulent.

Normally an outbreak suspected to be the result of criminal or terrorist attack would be investigated as a police matter by the country on whose territory it took place. However, in some instances, assistance under the protocol would be requested, e.g., if the affected country did not

have sufficient resources to mount an investigation, or if state-sponsored terrorism were suspected. Such investigations would also be conducted in a cooperative climate.

Outbreaks thought to be the result of attack by a nation on one of its own subnational groups or the result of an accidental release of harmful agents could lead to a request by one state party for an investigation on the territory of another. If the suspected nation is innocent of the allegations, it might cooperate fully with the investigating team. However, even for an innocent party, considerations of national sovereignty or concerns about revealing sensitive information about internal matters might incline the national government to oppose investigation under a convention protocol. Even the simple desire not to complicate an ongoing public health investigation could lead to reluctance; for example, the 1993 outbreak of hantavirus pulmonary syndrome in the United States had several highly suspicious features (7). Had the protocol been in force at that time, a request for an international on-site investigation, in parallel with the ongoing investigation of the Centers for Disease Control and Prevention, would have been likely. The United States would probably not have welcomed such a complication.

If the international community were to proceed with an unwelcome investigation, it would do so under decidedly uncooperative conditions. This could complicate and even compromise the investigation. Failure to cooperate with the investigation would constitute a violation of the protocol and could be interpreted as confirming guilt, an incentive to give at least the appearance of cooperation. The great difficulties that the U.N. Special Commission had performing facility inspections in Iraq with an uncooperative government remind us that actually implementing unwelcome investigations requires a daunting amount of political will and persistence (17-19). However, the success of the U.N. Special Commission in unearthing details of Iraqi weapons programs, despite failure of the Iraqi government to cooperate, shows that such investigations can be worthwhile.

Who Decides If an Outbreak Is Suspicious?

The negotiated protocol is expected to establish the Organization for the Prohibition of Biological Weapons, which will administer

certain aspects of the protocol, including investigations. An executive council composed of selected states parties to the protocol will authorize all investigations. Only states parties to the protocol will have standing to request an investigation.

This restricted standing could present a dilemma to public health professionals who might conclude from their investigation that an outbreak was deliberately instigated. For them, a professional approach would be to convey their suspicions and evidence to the organization sponsoring the investigation (typically the World Health Organization [WHO], a national or subnational health organization, or a nongovernmental organization). However, if the responsible organization is not willing to convey the suspicions to the government or to the Organization for the Prohibition of Biological Weapons, the public health experts may be in an awkward position, fraught with conflicting professional, political, and ethical responsibilities.

How a request from a state party for an outbreak investigation would be handled by the executive council is not yet clear. Existing precedents in arms control treaties are either of the "strong red light" or "strong green light" types. Under a strong red light mechanism, once a request is formally made, a substantial majority of the executive council must vote to oppose an investigation in order to stop it; otherwise, the investigation goes forward. Under a strong green light mechanism, once a request is made formally, a substantial majority of the executive council must vote in favor of an investigation in order for it to proceed. Both models raise concerns: the former because it may not provide sufficient protection from nuisance requests, and the latter because it may make investigating truly suspicious outbreaks very difficult if they are controversial.

The evidence brought to the executive council to support a request for an investigation is likely to be somewhat ambiguous, given the prevalence of natural outbreaks of disease. Its evaluation is thus not a trivial matter, and serious attention to this issue is warranted; two levels of analysis might be useful. First, the Organization for the Prohibition of Biological Weapons might assist the executive council by providing a technical analysis of the evidence. The organization is expected to have a staff of impartial experts in epidemiology and weapons control issues,

qualified to evaluate technical evidence. Second, each state party on the executive council should have a mechanism in place for consulting with its own experts on very short notice, since the executive council vote is expected to be mandated within a day of the request.

Sources of Information about Suspicious Outbreaks

Investigation of most suspicious outbreaks will be initiated by national or international public health agencies. In many cases the results of this initial public health investigation will implicate the outbreak as suspicious and provide the basis for a request for an investigation. The evidence should not be expected to be conclusive; however, it should provide reasonable grounds for suspicion that the outbreak may involve intentional or accidental release of prohibited materials. The investigation itself, once approved, will have the role of gathering sufficient additional evidence to decide if the suspicions are correct.

This evidence is likely to include one or more of the following: intelligence gathered by the state party requesting the investigation, epidemiologic data gathered by the state party requesting the investigation, or epidemiologic evidence gathered by an international organization (e.g., WHO). Other evidence could include recovered delivery devices and information gathered by nongovernmental organizations.

Intelligence information can be relevant when prohibited activities in a particular nation are suspected of causing an outbreak, and the intelligence directly addresses those activities. However, intelligence commonly requires substantial redaction to protect sources and capabilities, which can seriously compromise its persuasiveness. Thus, intelligence is unlikely to be a useful source of information for the executive council, except under unusual circumstances.

Commonly, relevant information suggesting that the outbreak is suspicious will be epidemiologic and will be obtained by a national or international health organization. If the source is a national health organization, the information can be expected to be freely available if the requesting party is the one that performed the investigation; if, however, a second party is requesting an investigation in a country that is unreceptive to it, the available information is likely to be limited and unreliable. Even when

freely shared, epidemiologic information from an interested party may not be complete and accurate.

Different problems are associated with epidemiologic information gathered by an international organization. Currently, for example, WHO's procedures prevent official release of information not approved by the host country. While permission to release information to the executive council would be expected when the host country and requesting country are the same, such permission would be unlikely if the host country opposed the investigation; nevertheless, the outlines of the results would likely be widely known, given the rapid expansion of epidemiologic information on the Internet (e.g., through ProMED Mail). However, the unavailability of official information could be a serious problem within the executive council, as it provides a credible rationale for questioning technical information.

As procedures are developed to share information among health organizations and the Organization for the Prohibition of Biological Weapons, the implications for public health need to be considered. The effectiveness of health organizations could be compromised if nations fear that a natural outbreak might be mistakenly judged suspicious. International health organizations will thus need to operate with great tact and caution when they encounter a potentially suspicious outbreak.

Finally, no matter how important the resolution of suspicions of convention noncompliance is, protecting ongoing public health response to an outbreak is essential. Containment of the outbreak and prompt treatment of patients cannot be compromised by a simultaneous arms control investigation.

Features of an Outbreak Investigation under a Biological and Toxin Weapons Convention Protocol

Most scientific aspects of an outbreak investigation in a Biological and Toxin Weapons Convention context are identical to those of a comparable investigation in a public health context. However, some striking differences occur because of the international scope and the quasi-forensic aspects of the investigation. While it is probably possible under most circumstances to discriminate between a natural (but unusual) outbreak, and one that results from accident or from intentional use (7), the acceptability of such

conclusions in a political context requires a high level of credibility.

The investigation's team leader will need to be a full-time member of the Organization for the Prohibition of Biological Weapons, with experience in supervising epidemiologic investigations and in handling the diplomatic issues of weapons control compliance. This leader will have to ensure scientific rigor, proper handling of evidence, impartiality, and tactful handling of publicity. Other members of the team will be chosen for their relevant expertise from the organization staff or a pre-approved list of experts employed outside the organization.

The possibility of interference from the host state makes it important that the team be as independent as possible. This is particularly critical for interpretative and translation services, but applies as well to such areas as communications, transportation, diagnostic reagents, standards, analytic equipment, and microbiologic media. Failure to ensure such independence may seriously compromise the effectiveness of investigations. However, the current draft protocol does not ensure independence of communications and transportation.

Unlike more routine investigations where sample tampering is not normally considered a risk, investigations of suspicious outbreaks will require strict documentation of the provenance and chain-of-custody of all samples. Sample analysis will require certifiably calibrated analytic equipment and standardized reagents. Such analysis should be done on-site or in approved diagnostic laboratories. Internal standards, replicate analysis, and blind testing should be used for the highest possible credibility of results.

Most investigations can be expected to overlap with ongoing public health investigations. There could thus be substantial difficulties in coordinating the two, with their very different goals and divergent requirements for sample handling and analysis. Information sharing will also be an issue, since both investigations need access to all relevant information about the outbreak, yet they must be independent.

Conclusions

For the public health community and their colleagues in plant and animal epidemiology, negotiating a protocol to the Biological and Toxin Weapons Convention will establish formal procedures for the investigation of certain outbreaks. These procedures will have certain elements, such as forensic standards for evidence handling, that are generally not familiar to field epidemiologists. However, the very formal procedures will help insulate scientists from the political dimensions of such investigations. Nevertheless, several aspects of the ongoing negotiations deserve the careful consideration of public health organizations and practitioners, for example, ways in which epidemiologic information gathered during a public health investigation can be used to justify a weapons-control investigation or to support or rebut the conclusions of such an investigation. Additionally, further consideration is needed about the implications of public health investigations' sharing personnel with highly politicized arms control investigations, a consequence of the small numbers of professionals with expertise in relevant disciplines.

The negotiated weapons convention protocol will improve security against biological attack. However, the costs to routine public health measures should be minimized to the greatest extent possible. This will require continued attention from both the arms control and the public health communities. Negotiations on the protocol are nearing the final stages in Geneva, and there is no longer opportunity for technical consideration to have much influence on the final language. However, advice from public health professionals will be needed as the detailed operating procedures are developed to implement the necessarily general diplomatic language of the new protocol. Such advice will be important at both the international level, as the Organization for the Prohibition of Biological Weapons develops detailed operating procedures, and at the national level, as each state party implements legislation and domestic operating procedures.²

²To learn more about the protocol and how to have input into the process, interested scientists can contact their professional organizations or nongovernmental organizations, such as the Federation of American Scientists (www.fas.org/bwc/), the University of Bradford Department of Peace Studies (www.brad.ac.uk/acad/sbtwc/), or the Monterey Institute of International Studies (<http://cns.miis.edu/research/cbw/>). All the relevant documents, including copies of the current rolling text of the Biological and Toxin Weapons Convention protocol, can be downloaded from these sites.

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