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Investigation Of Disease Outbreaks[1]

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Abstract. The Biological and Toxin Weapons Convention (BTWC) prohibits the development, production, and stockpiling of biological weapons agents or delivery devices for anything other than peaceful purposes. A critical aspect of any efforts to strengthen the BTWC would be provisions for the international investigation of outbreaks of disease that suggest a violation of the BTWC—outbreaks that may be the result of the use of biological weapons, or that suggest an escape from a laboratory conducting prohibited work. Such provisions are clearly useful from a weapons control viewpoint, but can present the international public health and epidemiology communities with significant problems. Active involvement of these communities in planning the implementation details of any system of disease investigations will be important for success.

1. Introduction

The Biological and Toxin Weapons Convention (BTWC)[2] prohibits the development, production, stockpiling, or transfer to other nations of biological weapons agents (microbial pathogens and toxins) for other than peaceful purposes, and any devices used to deliver these agents. Although the BTWC does not explicitly prohibit the *use* of biological weapons, it does so implicitly because any use presupposes prior production and stockpiling. The Convention was the first treaty to outlaw the development and possession of an entire category of weapon, and the first to outlaw any weapon of mass destruction. There are now 147 States Parties to the Convention, and an additional 17 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 United Nations Security Council, and further provides that 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.[3]

Recent information about the covert biological weapons programs of the former Soviet Union[4] and Iraq[5] added momentum to verification efforts begun in 1991. A draft text for a protocol to the BTWC was developed during negotiation over a period six year period culminating in the Composite Draft Text.[6] One of the provisions of the Draft Protocol is a mechanism for investigating certain outbreaks of disease, to resolve suspicions they might raise about compliance with the Convention.[7]

There are several reasons for such a mechanism.[8] 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 an 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 be expected to address and resolve such concerns. It would also deter the use of unsubstantiated accusations for propaganda purposes (e.g., the 1952 allegation of US use of biological agents in Korea and Manchuria[9]) and would reduce the credibility of fraudulent investigations controlled by the accuser. Finally, and perhaps most importantly, the political costs of being identified as a biological aggressor could deter covert biological weapons programs.[6,10]

2. 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 BTWC 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."[11] Thus very few outbreaks would likely become issues of treaty compliance.

An outbreak might be suspicious because epidemiological 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.[12] Also, the etiologic agent may differ from those that are 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 indicate 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.[6,8]

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 epidemiological 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] was suspicious largely because a number of putative delivery devices (balloons attached to meteorological 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 suspicious outbreaks will turn out to be natural occurrences.

3. 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: (1) covert biological attack by another nation; (2) criminal or terrorist attack; (3) covert attack by a nation on a subnational group within its borders; or (4) 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 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 may incline it to oppose investigation under international auspices. 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.[6] Had legally binding international measures been in force at that time, a request for an international on-site investigation, in parallel with the ongoing investigation of the US Centers for Disease Control, 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 could be interpreted as confirming guilt, an incentive to give at least the appearance of cooperation. The great difficulties that the UN Special Commission (UNSCOM) had performing facility inspections in Iraq with an uncooperative government reminds us that actually implementing unwelcome investigations requires a daunting amount of political will and persistence.[15] However, the success of UNSCOM in unearthing details of Iraqi weapons programs, despite failure of the Iraqi government to cooperate, shows that such investigations can be worthwhile.

4. Who decides if an outbreak is suspicious?

A BTWC Protocol would have established an organization to conduct investigations as well as other activities. An Executive Council composed of selected States Parties to the Protocol would have had the authority to authorize all investigations. Only States Parties to the Protocol would have standing to request an investigation. Other models to determine standing to request an investigation could be developed

Restricted standing to request an investigation 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 non-governmental organization). However, if the responsible organization is not willing to convey the suspicions to the government or an international institution, the public health experts may be in an awkward position, fraught with conflicting professional, political, and ethical responsibilities.

How a request for an investigation of a disease outbreak would be handled is not 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 forward 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, a number of impartial international experts in epidemiology and weapons control issues, qualified to evaluate technical evidence, might be available for consultation with international bodies. Second, states could have a mechanism in place for consulting with their own experts on very short notice since time may be of the essence in such investigations.

5. 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 provided by the state requesting the investigation; epidemiologic data gathered by the state 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 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 state performed the investigation; if, however, a second state requests 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 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 as it provides a credible rationale for questioning technical information.

As procedures are developed to share information among health organizations and those responsible for mounting and conducting investigations, 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.

6. Features of an outbreak investigation in an arms control context

Most scientific aspects of an outbreak investigation in an arms control 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,[6] the acceptability of such conclusions in a political context requires a high level of credibility.

The investigation team leader will need substantial experience in supervising epidemiologic investigations, and in handling the diplomatic dimensions 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.

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 and standards, analytic equipment and microbiologic media.. Failure to ensure such independence may seriously compromise the effectiveness of investigations.

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 pre-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.

7. Conclusion

Any formal procedures for the international investigation of certain disease outbreaks will have certain elements, such as forensic standards for evidence handling, that are generally not familiar to field epidemiologists. However, formal procedures will help insulate scientists from the political dimensions of such investigations. Nevertheless, several aspects to 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.

International investigations of disease outbreaks could contribute to improved 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. Advice from public health professionals will be needed as detailed operating procedures are developed. Such advice will be important at both the international level, and at the national level, as each state implements legislation and domestic operating procedures.[16]

Notes and References

[1] This is a revised version of: Wheelis, M. 2000. Investigation of outbreaks of disease under a Protocol to the Biological and Toxin Weapons Convention. *Emerging Infectious Diseases* 6, 595-600.

[2] *Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction*, opened for signature at Washington, London, and Moscow April 10, 1972; entered into force March 26, 1975.

[3] Chevrier, M. I., "From verification to strengthening compliance: prospects and challenges of the Biological Weapons Convention." Politics and the Life Sciences 14, 209-219 (1995); Kadlec, R. P., A. P. Zelicoff, and A. M. Vrtis, "Biological weapons control: prospects and implications for the future." JAMA 278, 351-356 (1997).

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[5] United Nations, "Report of the Secretary-General on the Status of the Implementation of the Special Commission's Plan for the Ongoing Monitoring and Verification of Iraq's Compliance with Relevant Parts of Section C of Security council Resolution 687 (1991)" S/1995/864, 11 October 1995. Annex.

[6] *Protocol to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction*. BWC/AD HOC GROUP/CRP.8/3 April 2001.

[7] United Nations, "Procedural Report of the Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction; Part I, Annex I, "Rolling Text of a Protocol to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction." BWC/AD HOC GROUP/50 (Part I), 4 February 2000.

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[15] Butler, R., *The Greatest Threat:Iraq, Weapons of Mass Destruction, and the Growing Crisis in Global Security*. New York: Public Affairs (2000); Trevan, T., *Saddam's Secrets: The Hunt for Iraq's Hidden Weapons*. London: HarperCollins (1999).

[16] Interested scientists can contact their professional organizations, or non-governmental 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 BTWC Protocol, can be downloaded from these sites.