

The Laboratory Response Network for Bioterrorism

SANDRA S HEATHERLEY

OBJECTIVE: To describe the function and levels of analysis performed by members of the Laboratory Response Network in coping with biological agents of terrorism.

DATA SOURCES: Current literature and the Internet.

CONCLUSIONS: The Laboratory Response Network is designed to enable rapid, safe, and accurate diagnosis of disease in order to mobilize the nation's response to acts of bioterrorism.

ABBREVIATIONS: APHL = Association of Public Health Laboratories; BSC = biological safety cabinet; BSL = biosafety level; BT = bioterrorism; CDC = Centers for Disease Control; LRN = Laboratory Response Network; SOP = standard operating procedure.

INDEX TERMS: bioterrorism; laboratory response network; safety.

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Sandra Heatherley MPH is the Director, Corpus Christi-Nueces County Public Health Department Laboratory and the owner of Quality Laboratory Consultants.

Address for Correspondence: Sandra Heatherley, Quality Laboratory Consultants, 518 Dolphin Pl, Corpus Christi TX 78411. 361-851-7214. sandrah@ci.corpus-christi.tx.us

Sandra Heatherley is the Focus: Management guest editor.

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Three and a half years ago the Congress of the United States mandated that a plan be developed to standardize laboratory procedures used for those reportable organisms which could become agents of bioterrorism. The result of that mandate is the Laboratory Response Network (LRN) developed by the cooperative efforts of the Association of Public Health Laboratories (APHL), the United States military medical facilities, and the Centers for Disease Control and Prevention (CDC).¹ Every practicing laboratorian has had an opportunity in the past three years to attend an organized continuing education or information-sharing session devoted to bioterrorism. These sessions have been and continue to be sponsored by a variety of professional societies; the CDC's National Laboratory Training Network; and federal, state, and local government agencies charged with emergency management and with law enforcement and investigative activities. Additionally the printed and electronic periodicals dedicated to the laboratory profession carried articles related to bioterrorism and the LRN months before the actual cases of *B. anthracis* were contracted by postal workers and citizens on the east coast. It is therefore assumed that the reader has some familiarity with the subject and the 18 cases of *B. anthracis* that were confirmed on November 21, 2001.

It is difficult to write about the LRN's organization, activities and intentions as understood prior to the autumn of last year when all of these were challenged with the reality of a biologic agent being used as a weapon. This article deals with those pre-October 11, 2001 intentions (yes, October) of the LRN and leads into the following articles that focus on lessons learned since the first cases of inhalational anthrax, mail-borne, were confirmed.

One concern that led to the creation of the LRN was the lack of standardization in Standard Operating Procedures (SOPs) among public health, hospital, and physician office laboratories.¹ While every accredited laboratory has SOPs, they are 'standard' only for that facility, network, or state. The goal of the LRN is to standardize procedures within the United States for the testing and referring of certain microbial specimen in order to hasten the identification of the microbes. This goal recognizes that speed in identification leads to early intervention and treatment in the event of a covert bioterrorist attack. The events of last fall did not fully test this ability since the sender of the anthrax spores did announce the intention to cause an infection in the text of the spore-laden letters. Therefore, it was not a totally covert attack. However, the previous prior planning efforts to create and empower the LRN were proven worthwhile as the events unfolded.

As with any new venture having close government ties, a vocabulary of initials and acronyms has emerged which can be confusing. The information in Table I will be helpful to those listening to or viewing presentations that relate to bioterrorism (BT). The term 'category' is used when speaking or writing about the disease agent. There are currently three categories defined, 'A', 'B', and 'C'.² These categories are characterized by:

- the ease with which an organism can be disseminated or transmitted person to person
- the degree of mortality, and potential for major public health impact
- the probability of public panic and social disruption
- the requirement for special action in order to achieve public health preparedness

By this definition the category A disease agents represent the highest priority and are those that pose the highest risk to national security. This category includes: anthrax (*Bacillus anthracis*); botulism (*Clostridium botulinum* toxin); plague (*Yersinia pestis*); smallpox (variola major); tularemia (*Francisella tularensis*); and viral hemorrhagic fevers.

Category B disease agents are the next priority and are:

- moderately easy to disseminate
- cause moderate morbidity and mortality
- require specific enhancement of surveillance and diagnostic capability

This category includes: brucellosis (*Brucella* species); epsilon toxin of *Clostridium perfringens*; glanders (*Burkholderia amillei*); Q fever (*Coxiella burnetii*); ricin toxin from *Ricinus communis* (castor beans); and staphylococcus enterotoxin B.

The third priority is category C and includes emerging pathogens that could be engineered for mass dissemination because of:

- availability
- ease of production
- potential for high mortality/morbidity and major health impact.

This category includes: hantaviruses; multidrug-resistant tuberculosis; nipha virus; tick-borne encephalitis viruses; and yellow fever.

In contrast, the term 'levels' is used to describe the laboratories in the LRN. There are presently four levels of laboratory participation defined, 'A', 'B', 'C', and 'D'. In this hierarchy laboratories occupy a level on the basis of the training, physical facilities, personal protective equipment, testing devices, and secured internet information available for analysts.

Fortunately the biosafety levels of the laboratories are expressed numerically (usually Arabic) in ascending order, so that level 1 requires no safety equipment and levels 2 through 4 require increasingly more stringent personal protective equipment and engineering controls. Biosafety level is usually written as 'BSL-1', 'BSL-2', etc. and spoken the same way.³ However, there are presenters and practitioners who refer to 'BL-1' or 'BL-4'.

The biological safety cabinet (BSC) is an essential barrier and air-handler for laboratories in the LRN. Biological safety cabinets are categorized by 'Class' and engineered to be 'Class I', 'Class-II', or 'Class-III'. These range in size and configuration from two-foot bench-top models to entire rooms. Categories, levels, class, numbers, and letters make up the notes that compose the music that is played by the symphony known as the LRN.

Level A laboratories work at a BSL-2 using a Class I or II BSC to **rule out** or refer BT agents. Currently this encompasses most hospital laboratories and city/county health department laboratories serving small or rural populations.

Level B laboratories work at a BSL-3 using a Class I or II BSC to **rule in** or refer BT agents. Level B laboratories have access to secured CDC web site information and access to analytic reagents not generally available to level A laboratories. At this writing, level B is represented by larger metropolitan city/county health departments and military hospital laboratory facilities.

Level C laboratories work at a BSL-3 plus added engineering controls and safety equipment using a Class I or II BSC to **rule in** or refer BT agents. Level C includes most State Health Department Laboratories and some military hospital laboratory facilities.

Level D laboratories work at BSL-4 plus even more engineering and safety features than level C to **rule in**, perform high-level characterization of disease agents, and archive the agents and information regarding them. Level D laboratories are at the CDC and the U.S. Army Medical Research Institute of Infectious Diseases (USAMRID).

Table 1. The LRN glossary of terms

Category A through Category C

Term used to describe possible disease agents

Level A through Level D

Term used to describe a laboratory's ability to rule out or identify a possible disease agent

Level 1 through Level 4

Term used to describe the biosafety precautions available to a laboratory

Class I through Class III

Term used to categorize the type of biological safety cabinet available to a laboratory

Even if the laboratory you are working in does not have a BSC but does perform microbiology, you are part of the LRN by virtue of the requirement to report and refer category A through C disease agents to state public health departments.⁴ If you are in a laboratory that refers all microbiology samples to a larger network laboratory or to a national reference laboratory, and serves a facility with an emergency room you are still part of the LRN. There is no rule that requires bioterrorism to be an urban event! There is no room for a 'choke' factor among laboratory workers, phlebotomists to PhD. Training and planning are the best enhancements to safety.

The experiences and 'lessons learned' from the autumn of 2001 are still being pondered and shared by healthcare workers, legislators, and law enforcement agencies. More than one state is considering increasing the capability of current level A laboratories to level B. The question of costs and who pays for these enhancements is a major management concern among mayors, city councils, commissioners of health, hospital administrators, etc. Currently CDC assumes the financial responsibility for reagents unique to level B laboratories while states, municipalities, and healthcare boards of trustees provide salaries and facilities for the LRN. The considerable costs of training and provision of information to the public and to laboratory practitioners are being accomplished by the federal government through the CDC on the Internet. This information is usually conveyed to the public by the local health department, and community health providers who can tap into the CDC resources on behalf of concerned citizens and the local media.

One of the lessons learned from last fall is that 'paper exercises' or simulated acts of bioterrorism are useful in preparing emergency response participants. However, the reports resulting from these simulations were far too optimistic about the degree of organization and communication that exists among the various responders and agencies. This fact is clarified with examples in the following article.

Whether it is a natural inkling or a learned behavior, microbiologists exhibit a 'do or die' approach to the identification of organisms isolated in 'their' laboratory from 'their' patients. The levels of the LRN are designed for speed and safety. Every level of laboratory has access to specific protocols for each category of biologic agent that may be used for bioterrorism. These are accessed via the bt.cdc.gov on the Worldwide Web. All but the level D laboratories are instructed regarding when and how to refer possible agents. Follow these protocols! The longer a culture is on the bench the greater the likelihood of exposure for laboratory workers. The last reported case of anthrax at this writing was on March 13, 2002 in a Texas laboratory worker. Speed is paramount and each step in the referral process depends upon timely and clear communication between the referring and receiving laboratories. Persons with the suspected disease and the public at large benefit from speedy referral and communication within the LRN and from the continued health of well-trained and vigilant laboratory service providers.

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