Applicability of Bioterrorism Preparedness in SARS: Focus on Laboratory Examination

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Abstract

To investigate the laboratory preparedness for bioterrorism, we studied the laboratories in 7 medical centers in Taipei that were implemented for SARS and compared with the laboratory requirements by the criteria of bioterrorism preparedness. Of seven medical centers in Taipei, one was categorized into Level A, four were categorized into Level C laboratories and two Level B ones. There were 100% of the laboratories possessing the capacity of bacterial and viral cultures, 100% microscopic examinations for all specimens, 44% electromicroscopic examinations, 100% serology such as FA and ELISA, 71% PCR, 71% HPLC, 86% GC, 100% general requirements, and 100% pathologic examination. Among them, one was categorized into Level A, five Level C laboratories and one Level B. The availabilities of laboratory equipments were the same as described. The major pitfall for all laboratories was the lack of personnel training for common agents for bioterrorism such as anthrax, smallpox and rabies. In conclusion, our survey revealed that the laboratory requirements were similar for both bioterrorism preparedness and SARS response. The laboratories in the medical centers could be considered to be designed under the "dual use" model. *(Ann Disaster Med. 2003;2:32-38)*

Key words: SARS; Bioterrorism; Laboratory; Hospital Preparedness

Introduction

For bioterrorism, early diagnosis can be critical to saving lives after a biological weapon release. Unfortunately, clinical diagnosis is often difficult because many of these diseases present initially as nonspecific febrile illness. Therefore, laboratory confirmation is particularly important with suspected biologic terrorism patients. The clinician should consider obtaining the samples for study.[1,2] Most laboratories can do the crucial initial evaluation with light microscopy, primary culture, and serology. Rapid antibody-based assay detector kits that can provide presumptive identification also have to be developed. A gene amplification assay such as polymerase chain reaction (PCR) is also an important part for the laboratory under such purposes.[3,4]

Severe acute respiratory syndrome (SARS) is a disease manifested by atypical pneumonia and rapid progression to respiratory distress.[5-10] It has been proven to be caused by the coronavirus.[11-13] In the viewpoint of disaster medicine, the preparedness for such an infectious disease should be similar to that for

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bioterrorism. Some diagnostic tools such as PCR,[11-13] indirect fluorescent antibody (FA) or enzyme-linked immunosorbent assay (ELISA) antibody have been rapidly developing,[13] although there are still many clinical difficulties in diagnosing the disease in a time-efficient manner.[14,15] The design and structure of the laboratories for SARS deserves to be investigated.

According to Advanced Health in America,[16] the hospital's patient care role begins with and follows the disaster. However, there have never been any events of bioterrorism or devastating infectious diseases such as SARS in recent decades. We therein retrospectively analyzed the design and structure of the laboratories for SARS in Taiwan and compared them with the laboratories for bioterrorism.

Methods

Requirements of the laboratory for bioterrorism

For comparison, we collected the information about the requirements of the laboratories for bioterrorism from related references.[11] The general recommendations for specimens to confirm a specific disease (caused by bioterrorism) include (1) Nasal and throat swabs or induced respiratory secretions for culture, FA, or PCR within 24 hours; (2) Serum for toxin assays; blood for PCR and culture; sputum for FA, PCR, and culture from 24 to 72 hours; and (3) Serum for toxin assays and IgM or IgG agglutination titers, blood and tissues for culture, and pathologic samples.

The classification of bioterrorism laboratories include:

Level A: These laboratories have a minimum biosafety level of BSL-2. They may be involved in early detection and will be capable of ruling out the priority agents of bioterrorism. They may be also capable of the presumptive identification of some of these organisms but will refer isolates to a level B reference laboratory.

Level B: These laboratories also have a minimum biosafety level of BSL-2. They are state public health and large private labs capable of definitive and rapid identification of organisms referred by Level A labs. They are also capable of a rapid response to announced events. These laboratories will rule in and refer organisms. When appropriate, Level B labs will forward specimens to higher level labs.

Level C: These laboratories are state public health, federal and academic labs capable of advanced diagnostic testing. These labs will have a minimum biosafety level of BSL-3. They also are capable of testing toxicity as well as evaluating new tests and reagents.

Level D: These laboratories are federal labs like the CDC and the military which have highly specialized capabilities for isolation and identification and have maximum containment facilities. They are capable of dealing with rare organisms such as Ebola and smallpox.

Requirements of the laboratory for SARS

According to the WHO, positive SARS diagnostic test findings depended upon (a) confirmed PCR for SARS virus (at least 2 different clinical specimens, or the same clinical specimen collected on 2 or more days during the course of the illness, or 2 different assays or repeat PCR using the original clinical sample on each occasion of testing); (b) seroconversion by

ELISA or indirect FA (negative antibody test on acute serum followed by positive antibody test on convalescent serum, or four-fold or greater rise in antibody titer between acute and convalescent phase sera tested in parallel); (c) virus isolation (isolation in cell culture of coronavirus from any specimen, plus PCR confirmation using a validated method.

Confirmation of positive PCR required appropriate negative and positive control in each run, which should yield the expected results, i.e., 1 negative control for the extraction procedure and 1 water control for the PCR run, 1 positive control for extraction and PCR run, and the patient sample spiked with a weak positive control to detect PCR inhibitory substances (inhibitory control). If a positive PCR result has been obtained, it should be confirmed by repeating the PCR using the original sample or having the same sample tested in a second laboratory. Amplifying a second genome region could further increase test specificity. It was recommended that reference laboratories should be identified at national level.

Data enrollment

We reviewed the data of 7 medical centers in Taipei provided by Department of Health, Taipei City Government. The checklist of laboratory equipment and guidelines were provided by Taiwan Center for Disease Control, which was actually modified from the WHO requirements (Table).

Statistical analysis

The categorical data were inputted in Microsoft Excel 2000 for descriptive statistics and further qualitative analysis. The correlation between the laboratory requirements evaluated by different criteria was made by a linear logistic regression model. A $P<0.05$ was considered to be statistically significant.

Results

Of seven medical centers in Taipei, one was categorized into Level A, four were categorized into Level C laboratories and two Level B ones.

According to the checklist derived from the Center for Disease Control, the presence of the cultures for bacteria and viruses was 100% (7/7), microscopic examinations for all specimens 100% (7/7), electromicroscopic examinations 44% (3/7), serology such as FA and ELISA 100% (7/7), PCR 71% (5/7), HPLC 71% (5/7), GC 86% (6/7), general requirements 100% (7/7), and pathologic examination 100% (7/7).

Table. Laboratory requirements for SARS (from CDC, Taiwan)

1. Cultures for bacteria and viruses
2. Microscopic examinations for all specimens
3. Electromicroscopic examination
4. Serology: direct / indirect FA; ELISA
5. PCR
6. toxin detection and qualification (HPLC, GC)
7. General laboratory requirements including CBC, biochemistry, coagulation profiles
8. Pathologic exmaination

ELISA: enzyme-linked immnosorbant assay; FA: fluorescent assay; HPLC: high performance liquid chromatography; GC: Gas chromatography; PCR: polymerase chain reaction

If checked by the requirements for bioterrorism, one was categorized into Level A, five Level C laboratories and one Level B. The availabilities of laboratory equipments were the same, that is, bacterial and virus cultures (100%), microscopic examinations (100%), electromicroscopic examinations, serology (100%), PCR (71%), HPLC (71%), GC (86%), general requirements (100%), and pathologic examination (100%). The major pitfall for all laboratories was the lack of personnel training for common agents for bioterrorism such as anthrax, smallpox and rabies.

Discussion

In the United States, the Center for Disease Control (CDC), in collaboration with the Association of Public Health Laboratories and the Federal Bureau of Investigation (FBI), established the Laboratory Response Network (LRN) to develop federal, state, and local public health laboratory capacity to respond to bioterrorism events.[4] This network is a strategic partnership designed to link front-line clinical microbiology laboratories in hospitals and other institutions to state and local public health laboratories and supports advanced capacities of public health, military, veterinary, agricultural, water and food-testing laboratories at the federal level. This partnership operates both domestically and internationally. Depending on a laboratory's ability to handle dangerous pathogens, the laboratory is designated either as a reference laboratory or a sentinel laboratory. Reference laboratories are the core, advanced technology laboratories that can provide confirmatory testing for agents in biosafety levels 3 and 4. This includes the centralized, state-of-the-art national reference laboratory located at CDC to rapidly and accurately identify any agent used in a biological terrorism attack (the Rapid Response and Advanced Technology Laboratory). Reference laboratories have access to a secure Website which allows for timely reporting and monitoring. These reference laboratories, which total about 120 laboratories, can access on-line agent protocols, share information, and order reagents. The estimated 25,000 sentinel laboratories play an important role in reporting possible outbreaks and ensure that specimens are sent to the appropriate reference laboratory for confirmation.

According to Advanced Health in America, Mass casualty incidents that result from infectious causes are different from all other types of incidents for many reasons, including: (1) the onset of the incident may remain unknown for several days before symptoms appear; (2) even when symptoms appear, they may be distributed throughout the community's health system and not be recognized immediately by any one provider or practitioner; (3) once identified, the initial symptoms are likely to mirror those of the flu or the common cold so that the health system will have to care for both those infected and the "worried well"; (4) having gone undetected for several days or a week, some infectious agents may already be in their "second wave" before the first wave of casualties is identified; (5) public confidence in government officials and health care authorities may be undermined by the initial uncertainty about the cause of and treatment for the outbreak; (6) health care authorities and hospitals may want to restrict those infected to a limited number of hospitals but the public may seek care from a wide range of practitioners

and institutions, and (7) health care workers may be reluctant to place themselves or family members at increased risk by reporting to work.

In a recent investigation from American Hospital Association[16] revealed that most of the hospitals in the United States were unprepared for bio-attack. In other words, most of the hospitals had emergency plans but lacked certain capacities for bioterrorism response. The percentage of urban hospitals that reported the laboratories specifying in emergency response plan to contact the specified entities during an emergency were 58.5% (range 34.0% to 75. 7% among different states). As the reports demonstrated, In order to be adequately prepared for bioterrorism, hospitals would need to have several basic capabilities, whether they possess them directly or have access to them through regional agreements. Plans that describe how hospitals would work with state and local officials to manage and coordinate an emergency response would need to be in place and to have been tested in an exercise, both at the state and local levels and at the regional level. Regional plans can help address capacity deficiencies by providing for the sharing, among hospitals and other community and state agencies and organizations, of resources that, while adequate for everyday needs, may be in short supply on a local level in an emergency. In addition, hospitals would need to be able to communicate easily with all organizations involved in the response as events unfold and critical information is acquired. Staff would need to be able to recognize and report to their state or local health department any illness patterns or diagnostic clues that might indicate an outbreak of a disease caused by a biological agent likely to be used by a terrorist. Finally, hospitals would need to have the capacity and staff necessary to treat large numbers of severely ill patients and limit the spread of infectious disease. They would need adequate stores of equipment and supplies, including medications, personal protective equipment, quarantine and isolation facilities, air handling and filtration equipment, and laboratory support.

Many of the capabilities required for responding to a large-scale bioterrorist attack are also required for response to naturally occurring disease outbreaks. Such a “dual-use” response infrastructure improves the capacity of local public health agencies to respond to all hazards. For example, a large-scale outbreak of SARS would require many of the same capabilities that would be needed to respond to an intentionally caused epidemic.

Our study revealed that the “dual-use” response infrastructure also could be applied in Taiwan. The laboratory requirements for bioterrorism and for SARS were similar. Most of the laboratories of the medical centers could provide similar supports for the above two purposes. Although there is still no evidence that the bioterrorism would occur in Taiwan, the laboratories constructed under such a “dual-use” infrastructure will be a good way for hospital preparedness.

In conclusion, our survey revealed that the laboratory requirements were similar for both bioterrorism preparedness and SARS response. The laboratories in the medical centers could be considered to be designed under the “dual use” model.

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