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Mobile laboratory in Sierra Leone during outbreak of Ebola: practices and implications

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Dear Editors,

Ebola virus disease (EVD) is an acute, serious and fatal illness caused by the Ebola virus. EVD was first identified in 1976 during two simultaneous outbreaks, one in Nzara, Sudan, and the other in Yambuku, Democratic Republic of Congo [1]. The latter occurred in a village near the Ebola River, from which the disease takes its name. Since its emergence, several EVD outbreaks have occurred in Africa. The 2013–2015 Ebola outbreak in West Africa is the largest and the most complex one to date. There have been more cases and deaths resulting from this outbreak than those reported for all previous outbreaks. The disease has also spread between countries, beginning in Guinea and then spreading across land borders to Sierra Leone and Liberia [2]. Of the countries afflicted, Guinea, Liberia and Sierra Leone have been the most severely affected; these countries also have very weak health systems, lack human and infrastructural resources, and have only recently emerged from long periods of conflict and instability, making control of the outbreak more challenging.

After emergence of the outbreak, numerious countries and organizations have provided assistance to aid in Ebola control. Ebola is transmitted through direct contact with patients or contaminated materials. Effective outbreak control relies on the application of a package of interventions, including case management, surveillance and contact tracing, good laboratory service, safe burials, and social mobilization.

Because Ebola is highly infectious and fatal, early diagnosis is key for patient isolation, treatment and transmission prevention. Confirmative diagnosis of EVD depends on laboratory diagnosis [3]. Because of the weak health system and infrastructure, West African countries have limited laboratory diagnosis capabilities, and all laboratory diagnosis are dependent on mobile laboratories from other countries. To summarize the laboratory practices and provide implications for future field diagnosis of emerging infectious diseases, we collected and analyzed information about mobile laboratories from the websites of the Health Department of Sierra Leone, World Health Organization (WHO), or other related organizations, or during laboratory exchanges.

EVD laboratory diagnosis includes non-specific diagnosis and specific diagnosis. Non-specific laboratory indicators of EVD include a low platelet count, an initially decreased white blood cell count followed by an increased white blood cell count; and abnormalities in blood clotting often consistent with disseminated intravascular coagulation (DIC) [4]. Confirmative diagnosis of EVD is based specific laboratory diagnosis. Confirmation of EVD includes isolating the virus, detecting its RNA or proteins, or detecting antibodies against the virus. Isolating the virus by cell culture, detecting the viral RNA by polymerase chain reaction (PCR) and detecting proteins by enzyme-linked immunosorbent assay (ELISA) are methods used to directly detect the pathogen. Detecting antibodies against the virus is an

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indirect method to show the infection. Although each of the available tests could provide confirmative information about the infection, these tests can only be used during an appropriate period of the infection (Table S1). Within days after experiencing symptoms, viral antigen and nucleic acid from the virus can be detected from in the blood or serum samples of patients. IgM antibodies are detectable two days after symptom onset and IgG antibodies can be detected 6–18 d after symptom onset. For corpse where blood sample is unavailable, oral swabs may be obtained and nucleic acid or viral isolation can be performed.

Since the outbreak of EVD, many countries and organizations have provided assistances in an attempt to control the outbreak in Sierra Leone. After March 2014, a total of 14 laboratories from 7 countries or organizations have been setup in Sierra Leone (Table S2). Of these laboratories, the Kenema Government Hospital Lassa Diagnosis Lab was the first laboratory to initiate Ebola diagnosis. However, this laboratory was shut down on August 7 2014 because of an infection in facility. Canada's lab started diagnosis early on July 2 2014. Their laboratory was located in Kailahun where Ebola was first transmitted from Guinea into Sierra Leone. England began its first laboratory in Kerry Town on October 28, and then in Port Loko and Makeni on December 6 and 10, respectively. China's mobile laboratory began EVD diagnosis on September 28. The European Union began three laboratories in December 2014, which moved from Liberia or Guinea where the incidence decreased near the end of the outbreak. Although there are several testes available for laboratory diagnosis of EVD, the most commonly used is real time PCR assay. All laboratories employed reverse transcription PCR (RT-PCR) assay to detect Ebola virus RNA. The WHO also defined PCR and real time PCR methods and protocols, including primers, probes and reaction conditions, to specifically detect the 2014 Ebola virus.

Of the mobile laboratories, those from the USA, China, South Africa and England, are mainly used for diagnosis. Samples were collected by sampling teams and sent to nearby laboratories. For sample reception and subsequent detection, laboratories have adopted different procedures (Table S3). For China Jui and England Port Loko, samples were received and stored to be tested in one or more batches of per day. For USA Bo and South Africa Lakka labs, samples were subjected to treatment and detection once received. These four labs have used different detection equipment and procedures. For Ebola diagnosis, samples were inactivated before subsequent analysis. Both heat and chemical inactivation were used by the four labs. Except for the China Jui lab, all labs employed only chemical inactivation. Nucleic acid extraction methods differed between labs. The Lakka lab used a manual extraction method, while the Bo lab used only automatic extraction; the other two labs used both manual and automatic methods. All the four labs used quantitative PCR (QPCR) to detect viral nucleic acids. In terms of the target choice, the Jui and Bo labs used a two-target detection strategy, and when either of the targets showed positive results, the sample was defined as Ebola infection-positive. The running time for each batch of sample ranged from 4–6 h. The human resources ranged from 4–12 persons, and the detection capacity per batch varied from 28–200 samples.

The China mobile laboratory was deployed in Freetown and began EVD diagnosis on September 28 2014. Because this was the first time a Chinese professional staff worked with this biosafety level 4 (BSL4) pathogen, great attention was placed on biosafety. The detection capacity during early stages was set to 24 samples per day. With proved skills and familiarity with the practice, the detection capacity steadily increased. To improve diagnosis quality and efficacy, a series of measures have been implemented (Table 1). For EVD diagnosis, an RT-PCR assay was developed to specifically detect the Zaire Ebola virus, and three RT-PCR kits were licensed for an urgent evaluation. These kits provided highly qualified diagnostic reagents for the laboratory. In addition to the diagnostic kit, many other measures have been undertaken to improve quality and efficacy. These measures included sample reception, pre-treatment, nucleic acid extraction, amplification and case definition criteria. To improve information check efficacy, samples and their information were photographed and then checked by staff outside of the BSL3 cabinet. An automatic nucleic acid extraction machine was introduced to improve extraction efficacy. With these optimizations, the detection capac-

Table 1 Improvement of detection quality and efficacy by China mobile laboratory

Factors restricting efficacy and quality	Efficacy improvement measures	Improved quality or efficacy
Quality		
Protocol and adherence	Strict training and exercise	All persons strictly adhere to protocols, ensuring quality
Amplification	Two target, replicate, in-house control	Reducing possibility of false positive or negative
Result interpretation	Combining raw data, curve and duplicates	Generate confirmative results
Efficacy		
Sample number instable	Coordinate sample sending	Sample number was increased and relative stable
Complicated sample information check	Photographed and sent outside of P3 for checking	Checking time was reduced over 75%
Capacity of heat Inactivation	Heat inactivation with high capacity incubator	Batch capacity improved 3 times
Manual extraction	Replacement with automatic robot	Batch capacity improved 4 times and time reduced 60%

ity was increased to at least 200 samples per day. Because of these improvements, the China mobile laboratory successfully passed the external quality control assessment initiated by the WHO with 100% accuracy, making it one of the most high-performance labs participating the assessment.

Because the Ebola virus is a BSL4 pathogen, biosafety is extremely important to the staff handling the samples. During the outbreak, we visited the US Bo, England Port Loko and South Africa Lakka laboratories. These laboratories used different biosafety countermeasures. As shown in Table S4, there were differences in personal protection equipment, laboratory protection level, sample inactivation, and high-throughput diagnosis. Ebola virus is a pathogen that should be manipulated under BSL4 condition, however, under field conditions, it is difficult to completely meet these criterion. Labs from South Africa and England used negative pressure biosafety gloves, while the China lab used BSL3 mobile laboratory. Surprisingly, that the US Centers for Disease Control and Prevention (CDC) labs did not use any biosafety equipment, the only protections included gloves and visors. All labs used automatic extraction robots. The US CDC used two types of extraction machines, 15-sample and 96-sample automatic extraction machines. The 15-sample machine was used for small batches of samples, while 96-sample machine for large batches. The China Lab adopted level A protection, which is complicated and expensive. Because of the relatively complicated procedures, the China lab diagnosed only 1–2 batches of samples per day.

Our analysis and summary of mobile laboratory practices are important for our future works. The 2013–2015 EVD outbreak in West Africa is the most severe public health disaster in recent years. China, has begun to have increasingly important roles in international affairs. Since the outbreak occurred, China participated in the international campaign against the disaster, which was a valuable opportunity for China's public health professions. The Ebola control and prevention mission represented many firsts for China's public health professions: the first public health action oversea, first handling a level 4 pathogen, and first time extending control front against an infectious disease to oversea. Before this outbreak, we had no experience with the control of infectious diseases overseas. We must face many new challenges, ensuring our mobile laboratory is safe, cooperating and/or competing with labs from other countries, cooperating with the local health department.

We have successfully setup our mobile laboratory in Freetown, Sierra Leone. Through systematic optimization and improvement in diagnosis procedures and protocols, we significantly improved the diagnosis quality and efficacy. Our detection capacity has steadily increased and is comparable to or higher than that of labs from other countries. We diagnosed approximately 20% of the total samples in the whole country. We successfully passed the external quality control test with 100% accuracy in the shortest amount of time. During this test, two of the six participating labs did not pass the assessment with 100% accuracy. This indicated the high quality and efficacy of our mobile laboratory.

Although we successfully participated in the campaign against EVD outbreaks, we also faced challenges. Ebola was first discovered in 1976, although approximately forty years have passed, there has been no significant scientific improvement in understanding of this disease in our country, while America has invested in not only basic research, but also in the prevention and control of outbreaks.

EVD diagnosis in West Africa is mainly dependent on RT-PCR assays, which include sample inactivation, nucleic acid extraction and amplification. The complete process requires 4–6 h, which is a relatively long period of time for the highly infectious, fatal and rapid progress EVD. Point-of-care diagnosis assays are urgently needed. However, there are no commercial reagents for these diagnosis assays for EVD.

Taken together, mobile laboratories have played important roles in the identification and control of EVD outbreak. Through the use of our mobile laboratory, we have accumulated much experience with field laboratory diagnosis. Good practice from other laboratories will be valuable for our in future work.

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Supporting Information

Table S1 Available diagnosis tests with timeline of infection

Table S2 Mobile laboratories in Sierra Leone during the EVD outbreak

Table S3 Comparisons of virus detection between four main field labs

Table S4 Biosafety protection and cost comparisons between four laboratories

The supporting information is available online at life.scichina.com and link.springer.com. The supporting materials are published as submitted, without typesetting or editing. The responsibility for scientific accuracy and content remains entirely with the authors.