Urgently needed: rapid, sensitive, safe & simple Ebola diagnostic tests

Laboratory support is crucial to interrupting transmission of Ebola virus transmission: to confirm suspected cases, guide triage and clinical decisions, aid contact tracing and facilitate early detection of cases in people with previous exposure. It also underpins effective case detection and quarantining of patients.

But efforts to contain the Ebola outbreaks in West Africa are currently hampered by cumbersome, slow, complex and costly diagnostic tests.

The standard molecular assays currently used in mobile and other laboratories supporting the Ebola response include the reverse-transcriptase polymerase chain reaction, or RT-PCR test. This test provides very accurate results when performed by trained staff with expertise in using sophisticated machines. But it involves a number of laborious procedures, requires a full tube of blood, takes from 2 to 6 hours, costs around US$ 100 and demands a high level of laboratory biosafety. Meeting these requirements is difficult, if not impossible, in resource-constrained West African settings, thus severely limiting testing capacity.

Lost time – for patients and treatments

Transporting patient samples over bad roads to West Africa’s limited number of laboratories takes time and means that anxious patients and their families may need to wait several days for test results.

Lost time means that infected people may remain in the community, at severe risk of unknowingly transmitting the virus to others. And in the absence of rapid laboratory testing, people with other common infectious diseases, such as malaria and dengue, who have symptoms that are similar to those for Ebola, may be unjustifiably held in an Ebola “transit” centre as a precautionary measure. If they did not have Ebola when entering the centre, they may unfortunately contract it there.

Apart from posing a severe risk to families and communities, undiagnosed and unmanaged patients contribute to the cyclical transmission pattern currently being seen, whereby cases begin to fall as control measures take effect, only to spike again as new chains of transmission are ignited.

Perhaps most importantly, a recent research study, based on the management of more than 700 Ebola patients in Monrovia, Liberia, strongly suggests that clinical decisions guided by results from rapid point-of-care diagnostic tests could significantly improve treatment outcomes.

Moreover, having such tests readily available could restore some order to West African health systems, which have been devastated by fear of contagion as well as by the demands of managing a deadly and dreaded disease.

WHO initiatives to stimulate diagnostic innovation and deployment of suitable tests

For all these reasons, WHO has launched two urgent initiatives to stimulate diagnostic innovation and expedite the delivery of better and faster tests to West African countries –
compressed into months instead of years. The first initiative is moving forward in close collaboration with manufacturers, academic researchers, staff from the charity Doctors without Borders, or MSF, and the non-profit organization Foundation for Innovative New Diagnostics, or FIND.

With its partners, WHO is working to minimize the barriers faced by diagnostic companies to develop and deploy their test by clearly defining the needs, by identifying channels to access early validation materials and clinical samples for research and development, and by preparing the deployment of these new tests in the affected countries.

The “ideal” molecular assay

To clearly define the needs and thus guide the development of tests, WHO issued a detailed profile of the “ideal” rapid, sensitive, safe and simple diagnostic test considered most likely to accelerate interruption of virus transmission in severely resource-constrained settings.

http://www.who.int/medicines/emp_ebola_section/en/

For example, the ideal test should be suited for use in peripheral health clinics with no laboratory infrastructure in place. Testing procedures should involve fewer than three steps, produce results in less than 30 minutes, and have no biosafety requirements beyond the wearing of personal protective equipment.

Additional operational specifications pertain to the easy storage and reconstitution of reagents and staff training that takes less than half a day. The ideal test and related portable equipment should need no power supply and require no maintenance.

In the absence of regulatory oversight of most commercial Ebola tests, WHO is also assessing the quality of these tests. To date, no rapid tests, either on the market or under development, have undergone full regulatory assessment, underscoring the need for an independent review of these products before they are used in the field. Some tests are marketed for research use only, and not for use with patients.

The second WHO initiative is the establishment of the Emergency Quality Assessment Mechanism, a rapid review process for assessment of a diagnostic’s quality, safety and performance. An early-October invitation was sent to manufacturers known to be working on diagnostic tests for Ebola virus, to submit documentation containing evidence they have compiled relating to the safety, quality and performance of the diagnostic. Information to be submitted includes the recommended specimen types; evidence of test performance, including sensitivity and specificity; suppliers of critical components or raw materials and services, and data on current inventory and manufacturing capacity and quality.

Sixteen sets of documentation were received by mid-October. These include conventional RT-PCR diagnostic kits, automated “desktop” PCR systems with integrated specimen processing, and new point-of-care tests that could – within minutes – detect Ebola virus infection with blood from a finger-prick instead of a full tube. The documentation is independently assessed for WHO by expert virologists and the most promising tests will be subjected to a rapid laboratory evaluation using clinical specimens to verify performance.

The emergency quality assurance mechanism is currently assessing the first five of the 16 documentation sets submitted to date. Australian, Belgian, and Dutch reviewers are
participating in the evaluation, together with staff from the WHO Prequalification of In Vitro Diagnostics Programme. The overarching objective is to guide bulk procurement decisions by WHO and other partners that will get the best tests to West Africa within the next few months. This work is being supported by the Bill and Melinda Gates Foundation.

The good news

As WHO has noted, the development of rapid and simple to use assays is technically readily achievable. Their commercial price is expected to be less costly that conventional PCR tests. Biomarkers already exist. No significant technical hurdles stand in the way.

Further progress and outstanding needs will be discussed during a WHO expert consultation on innovative Ebola diagnostic tests to be held in Geneva in December.