WHO-ISARIC joint MERS-CoV Outbreak Readiness Workshop:  
Clinical management and potential use of convalescent plasma  
10-12 December 2013

The meeting, held on 10-12 December 2013 in Geneva, brought together clinicians with experience in caring for patients with MERS-CoV infection and multidisciplinary experts from affected countries (France, Jordan, Qatar, Saudi Arabia, Tunisia, United Arab Emirates and the United Kingdom), technical experts from institutions conducting pre-clinical research to support the clinical community, as well as members of the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC)\(^1\), the co-organizer of the meeting. The meeting was an important opportunity to learn from first-hand experiences, and to discuss potential therapeutic interventions.

The case-fatality rate of MERS-CoV infection is still high, approaching 50% among hospitalized patients. In addition, at present no specific vaccines or antivirals are available. The focus of discussion was on obtaining better data on disease pathogenesis and therapeutic options. The importance of prospectively collecting standardized clinical, virologic, and other biologic data over time from affected patients, and working towards implementing studies with anti-MERS-CoV antibodies, initially in the form of convalescent plasma, was emphasized.

To assist in this process, the WHO Ethics Review Committee recently approved WHO-ISARIC MERS-CoV natural history and biological sampling protocols and associated case report forms, information and consent documents to enable collection of data in a standardized manner across a range of resource settings. The pre-approved master protocols are expected to expedite national, local or institutional review board ethics approval. Systematic data collection will be essential to combining data for analysis from different clinical sites. These documents are currently available on both WHO and ISARIC websites\(^2\).

In the absence of specific therapy of proven effectiveness for MERS-CoV, the rapid clinical progression of the severe disease in hospitalized patients suggests that timely use of an effective antiviral could reduce mortality.

A WHO-commissioned systematic review conducted by Nottingham University of data on use of convalescent plasma and other blood products in influenza and SARS-CoV infections supported the conclusion that convalescent plasma is a particularly promising intervention that warrants careful clinical study in MERS-CoV infections.

\(^1\) http://isaric.tghn.org/  
\(^2\) http://www.prognosis.org/isaric/
Efforts to develop highly neutralizing antibody preparations against MERS-CoV (monoclonals, transgenic cow-derived human polyclonal antibodies) are moving forward and may offer additional therapeutic options in 2014.

Currently approved drugs for other indications are being screened by several groups to assess their anti-MERS-CoV activity in pre-clinical studies, and improved animal models are being developed. Once shown to have in vivo activity at relevant doses in such models, one or more of these drugs would also be candidates for controlled testing in affected patients.

The participants agreed to work towards developing a regional clinical research network and agreed on: 1) conducting a feasibility survey in the countries to identify suitable sites and current capacities for clinical research studies, 2) developing a multi-center retrospective case series and prospective study to characterize the disease course, prognostic factors, and outcomes with current treatment approaches, 3) exploring local processes for convalescent plasma collection from MERS-CoV-infected patients (directed donations) and using it as a therapeutic intervention in the context of a prospective observational study with serial virologic sampling, and 4) developing a randomized controlled trial of an antiviral intervention (convalescent plasma in the first instance) if larger numbers of cases occur.