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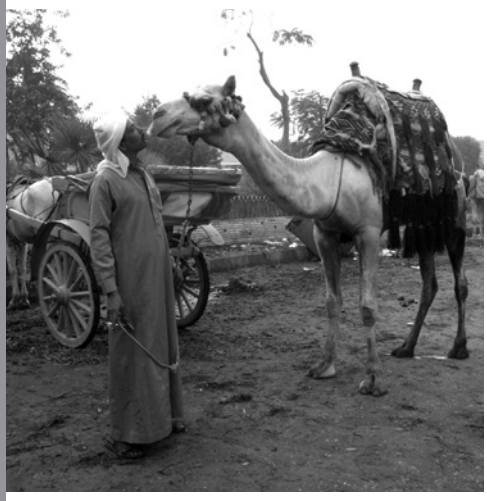
FAO ANIMAL PRODUCTION AND HEALTH



report

UNDERSTANDING MERS-CoV AT THE ANIMAL-HUMAN INTERFACE

Technical meeting
21-22 January 2016
Rome, Italy

11

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Abbreviations & Acronyms

CIRAD	Agricultural Research Institute for Development, France
CoV	Coronavirus
ECTAD	Emergency Centre for Transboundary Animal Diseases, FAO
ELISA	Enzyme-Linked Immunosorbent Assay
EMC	Erasmus Medical Centre, the Netherlands
EPT	Emerging Pandemic Threat
FAO	Food and Agriculture Organization of the United Nations
HKU	University of Hong Kong
HQ	Headquarters
ICPALD	IGAD Centre for Pastoral Areas and Livestock Development, Kenya
IGAD	Intergovernmental Authority on Development, Republic of Djibouti
KEMRI	Kenya Medical Research Institute
KSA	Kingdom of Saudi Arabia
MoA	Ministry of Agriculture
MoH	Ministry of Health
MERS	Middle East Respiratory Syndrome
NRC	National Research Centre, Egypt
OIE	World Organisation for Animal Health
PCR	Polymerase Chain Reaction
ppNT	Spike Pseudoparticle Neutralization Test
RNA	Ribonucleic Acid
RT-PCR	Reverse Transcription Polymerase Chain Reaction
SAR	Special Administrative Region
SOP	Standard Operating Procedure
TWG	Technical Working Group
USAID	United States Agency for International Development
VI	Virus Isolation
WHO	World Health Organization

Introduction

The Technical Meeting on understanding Middle East Respiratory Syndrome Coronavirus (MERS-CoV) at the human-animal interface was convened by the Food and Agriculture Organization of the United Nations (FAO) to determine the current status of scientific knowledge on MERS-CoV and identify major gaps that require further studies, in order to better understand the disease dynamics at the interface between humans and animals, and to develop practical approaches to control and minimize the impact of this virus. The meeting also aimed at fostering collaboration and partnerships between institutions and organizations working on MERS-CoV at the human-animal interface. It was held in Rome from 21-22 January 2016, and was attended by 64 participants from Egypt, France, Germany, Hong Kong Special Administrative Region (SAR), Israel, Jordan, Kingdom of Saudi Arabia, The Netherlands, Qatar, United Arab Emirates, the United Kingdom and the United States, and from EcoHealth Alliance, Metabiota, International Medical Corps, the World Organisation for Animal Health (OIE), the International Atomic Energy Agency (IAEA), the Intergovernmental Authority on Development (IGAD), the International Livestock Research Institute (ILRI), the European Food Safety Authority (EFSA) and FAO. This report provides the key objectives for the meeting and summarizes major outputs that include the gaps and needs identified, and the main recommendations made by the meeting participants.

BACKGROUND

Middle East respiratory syndrome coronavirus (MERS-CoV) can cause severe pneumonia in humans and is considered an emerging global public health threat. The disease was first detected in Saudi Arabia in 2012, and as of 3 February 2016, the WHO has been notified of 1 638 laboratory-confirmed human cases, including 587 fatalities. MERS-CoV has also been isolated from dromedary camels in several countries in the Near East and East Africa and antibodies to MERS-CoV have also been identified in very high proportions of camels in a number of countries across the Horn of Africa, North Africa and in the Near East.

Evidence suggests that primary human cases might have been exposed to the virus through contact with an animal host, and several studies have shown dromedary camels to be a source of human infection. Molecular similarities between other β-CoVs identified in bats and MERS-CoV isolated from camels and human patients point to the possibility of a bat reservoir. Critical gaps remain in our knowledge of many aspects of the epidemiology, ecology, and pathogenesis of MERS-CoV.

A number of research groups are currently investigating various aspects of MERS-CoV, and significant scientific information has been published during the past three years. FAO is embarking on a field programme to investigate MERS-CoV along the animal value chains in the Horn of Africa, North Africa and the Near East to better understand the disease dynamics at the animal-human interface. In this regard, FAO convened a technical meeting to determine the extent of

current scientific knowledge, identify the major study gaps, and develop practical and realistic approaches to minimize the risk of transmission to humans and reduce the adverse impacts of this virus.

MEETING OBJECTIVES

1. Share information on ongoing studies on the role of livestock and wildlife in the epidemiology of MERS-CoV.
2. Identify and prioritize knowledge gaps in disease dynamics at the human-wildlife-domestic animal interface.
3. Peer-review scientific and technical approaches on MERS-CoV at the human-animal interface, including the dynamics of viral emergence and evolution, surveillance design, diagnostics, and risk factors along animal value chains.
4. Analyse complementarities and synergies between programmes and projects implemented by various partners, and explore opportunities for collaboration and partnerships.

Knowledge gaps

EPIDEMIOLOGY AND RISK FACTORS

Antibody kinetics and immunity in camels

- Antibody kinetics in camels are unknown.
- Mode of protective immune response and duration of immunity are not fully elucidated.
- Whether re-infection of camels results in virus shedding, and if re-exposure leads to more robust immunity.

Shedding patterns

- Viral replication is mainly restricted to the (upper) respiratory tract of camels; however, RNA has also been found in camel milk. The source of viral RNA in milk is unknown (haematogenous or contamination from suckling calves), and the risk of transmission from this and other sources has not been established.
- Although evidence suggests that live virus cannot be found in other bodily secretions, this should be further investigated, especially in the light of the consumption of camel urine in some countries.

Surveillance

- Antibodies to MERS-CoV have been found to be highly prevalent in camel populations in many countries but knowledge of the geographical distribution of seropositive camels and other animals is not complete in parts of Africa and central Asia.
- Details of viral circulation in camels is largely unknown, including risk factors for transmission, such as production systems, herd size and management, seasonality and camel-level risk factors such as age, sex, immunosuppression, and co-infection.
- The naturally infected host range has not been fully explored.
- Origin of the virus is still unknown.

Case definitions and regulatory issues

- Case definition for reporting MERS-CoV in animals has to be redefined as it is clear that not all polymerase chain reaction (PCR) positive animals are necessarily shedding infectious viruses.
- Risk communication is difficult in view of the fact that the risk of a PCR positive animal in terms of onwards animal transmission and human exposure is difficult to determine.
- The trade and regulatory implications of PCR positive animals have not been explored. For example:
  - how positive animals found during active surveillance are reported;
  - what are the quarantine recommendations for PCR positive animals;
  - what are the differences between farm level and cross-border implications of positive animals;

- What is the implication of PCR positive animals in different epidemiological (routine investigations, investigation around human cases, etc.) and production contexts (farms animals, trade animals, transhumant, racing, etc…).

Epidemiology of MERS-CoV in humans

- To date, there are no reports of any acute human MERS-CoV cases in Africa, and yet a high level of seroprevalence is observed in camel populations, while one survey has shown a low level of seroprevalence in human populations.
- The reasons for the lack of reported human cases in Africa is unknown. The possible reasons identified were: missed/under-reported cases, host susceptibility, genetic differences of the virus, asymptomatic population, differences in human behaviour and healthcare systems.

LABORATORY DIAGNOSTICS

Serological tools

- Commercial Enzyme-Linked Immunosorbent Assays (ELISA) are available for camel and human diagnosis. However, sensitivity and specificity of the assays have to be assessed more accurately.
- ELISA for multispecies testing is not available. Control sera for proper test validation are needed.
- Development and validation of a rapid test for camels and/or other animal species.
- Alternative confirmatory tests that do not require virus culture are needed. Only few laboratories are able to carry out tissue culture-based tests, due to the need to use BSL3 facilities. An existing test, based on the spike pseudoparticle neutralization test (ppNT), could be validated, and a confirmatory ELISA or Western blot test developed.

Testing algorithms

- Testing algorithms and Standard Operating Procedures (SOPs) are not available.
- OIE is currently processing certification for a newly developed rapid test. However, the introduction of this test in the testing algorithm needs to be evaluated.

Molecular tests and molecular epidemiology

- Many different PCR protocols are used. It is important to find out if all protocols are adapted to the circulating strains.
- Few sample types (sera, tissue, etc.) from different species (human, wildlife, domestic animals) exist for further molecular studies.
- Field samples often lack the quality necessary for sequencing.
- Molecular markers of virulence or potential for zoonotic transmission are not well known.

Pathogenesis and experimental infections

- The relation between pathogenesis and the PCR and/or serological results is not well understood.

- The circulating viruses are not well characterized genetically. Experimental infections with various strains are needed for phenotype determination.

Camel vaccines

- Novel camel vaccines and modalities for effective vaccination (preventing MERS-CoV transmission), need to be further investigated.
- Where and how often should vaccines be targeted for effective intervention? (e.g. at what age, which camel populations, how frequently, is a booster needed, and how often will it have to be applied?) At what age would they be useful? Which protocol should be used and will they be culturally acceptable? Which animal population should be targeted?
- The issues surrounding a camel vaccine for public health should be explored: How to make it acceptable to camel owners, who pays for the vaccine, etc… (is the objective of vaccination only to protect public health)? Can MERS-CoV be combined with other vaccines (Rabies)? Yes, according to the Erasmus group.

VALUE CHAIN AND BEHAVIOUR STUDIES

The camel sector is generally neglected compared to other livestock sectors, in terms of governance, regulations, and professional associations. This has led to a lack of readily accessible data on camel value chains. Economic drivers, as well as the supply and demand of camels, camel products, and camel feed are all little known.

Production Systems

- There is a lack of accurate numbers on overall camel populations and within each camel sector (dairy, racing, meat, etc…).
- Characterization of the production systems including intensive/extensive raising, herd sizes, other species raised, and seasonality is needed.
- Regional differences in camel raising and production systems are unknown.

Trade

- The camel sector is largely unregulated. It is therefore difficult to access the organization and structure of the value chain, and quantify camel movements in formal trade. Furthermore, informal trade is common but extremely difficult to quantify or estimate.
- There is no formal system of traceability or camel identification.

Human behaviour and culture

- Risky behaviours for disease transmission are not fully characterized, such as those activities specific to different camel sectors (racing, milking, slaughter, etc…).
- Gender roles and responsibilities in the different camel sectors and regional differences are poorly described or little known.
- The impact of culture, values and social status on camel value chains is not well known, such as transhumance routes and trade and religious or cultural festivals.
- Disease knowledge and risk perceptions among key populations have not been explored.

Addressing needs and knowledge gaps

Conclusions were summarized and specific action points highlighted.

COORDINATION

- Strengthen NATIONAL multisectoral/One Health platforms for MERS-CoV at the human-animal interface for information sharing, surveillance and joint outbreak investigations.
- Improve and expand INTERNATIONAL collaboration and platforms under the FAO/OIE/WHO tripartite in liaison with other global and regional partners to share knowledge, data, biological material, etc.
- Identify and disseminate methodologies/approaches that are culturally sensitive, build trust and encourage cooperation of local communities for the conduct of field activities.

EPIDEMIOLOGY

- Conduct additional research to identify environmental and other ecological risk factors and geographic distribution.
- Conduct additional research to identify human behaviours that affect transmission.
- Update case definitions for animals and herds based on recent research findings.
- Develop guidelines for joint outbreak animal/human investigations.

LABORATORY DIAGNOSTICS

- Develop testing algorithms and SOPs for field sampling and testing of MERS-CoV across species and countries.
- Conduct infection experiments to understand pathogenesis and immunity in different animal species.
- Conduct molecular studies for further virus characterization.
- Conduct Bayesian studies to evaluate and compare the performance of diagnostic tests.
- Create a virtual and physical biobank as a shared resource for specimens and standards.

VALUE CHAIN AND BEHAVIOURAL STUDIES

- Identify critical control and intervention points along livestock value and supply chains to inform surveillance, policy, and risk management.
- Identify appropriate behaviour change options to reduce spillover and zoonotic disease transmission risk.
- Formulate risk communication messages and strategies regarding PCR-positive animals.

Activities undertaken by participating partners

- Kingdom of Saudi Arabia (KSA), Ministry of Agriculture (MoA) and Ministry of Health (MoH): Longitudinal study in camels and in-contact humans, wild animal species testing in areas with human cases.
- Israel: camel serology (60 percent seroprevalence).
- ILRI and local partners such as Kenya Medical Research Institute (KEMRI), Kenya Veterinary Services, Kenya Wildlife Services, CIRAD, PREDICT-2 and Jordan Veterinary Services: virus prevalence studies (PCR and virus isolation - VI), livestock and wildlife serology, longitudinal studies in select camel herds.
- PREDICT-2 (Metabiota, EcoHealth Alliance, UC Davis): biological surveillance in wildlife, humans and domestic animals, diagnostic capacity development.
- CIRAD and Hong Kong University (HKU): Longitudinal study, camel sampling at abattoirs and farms, with human and bat sampling, virus characterization, transmission modelling, studies on 5 000 camels in Burkina Faso, Morocco, Sudan, Kazakhstan (herd management, size, etc.).
- MoA of KSA and Erasmus Medical Centre (EMC): vaccine filed trials in female camels and studies of the effects on offspring.
- IGAD Centre for Pastoral Areas and Livestock Development (ICPALD) in collaboration with AU-IBAR and FAO (Emergency Centre for Transboundary Animal Diseases - ECTAD): Regional stakeholders workshop held in October 2015 with the objectives to create awareness on MERS-CoV and develop a roadmap for enhancing surveillance, improving diagnostic capacities, furthering research and enhancing coordination. The IGAD region is a major camel producing and exporting area. As a result of the workshop, a technical working group (TWG) has been established to oversee and coordinate MERS-CoV activities in the region, and mobilize resources.
- Egypt National Research Centre (NRC) and FAO (ECTAD): A cross sectional study in camels and other livestock species showed that seropravalence in camels is 73 percent. A longitudinal study is planned.

Action points

- FAO to consult with EPT2 Preparedness and Response (P&R) to assist the creation/strengthening of national One Health platforms and reinforce networks by running simulation exercises for different scenarios, etc.
- FAO to continue to provide opportunities for international scientific and field discussions/meetings (physical and virtual) to fill in knowledge gaps, develop guidance documents, share information, and standardize approaches.
- FAO to involve local research institutions and organizations in EPT-2 activities.
- FAO to facilitate policy dialogue (for different issues/levels).
- FAO to coordinate development and refinement of laboratory tests.
- FAO to create an international scientific network of expertise for MERS-CoV together with the OIE and in close consultation with WHO for public health issues.
- FAO to foster collaboration and partnerships with and between research institutions and local organizations.
- Study to be conducted on defining camel farming systems in East Africa and the Gulf countries, comparing patterns and characterizing risky human behaviour.
- Use of harmonized methodologies for field studies in order to facilitate comparison of results.
- FAO to support Regional Technical Working group on MERS-CoV such as in the IGAD region /Greater Horn of Africa.

Annex 1
Agenda

AGENDA

Understanding **MERS-CoV** at the **animal-human interface**

Technical Meeting
Rome, Italy • 21-22 January 2016

Food and Agriculture Organization of the United Nations

21 January Thursday

08:30-09:00	Morning coffee and registration
09:00-09:30	Welcome, introductions and expectations
09:30-10:15	Scientific overview presentations: • Epidemiology and risk factors *(15 min.)* • Laboratory diagnosis *(15 min.)* • Supply chains and behavioural studies *(15 min.)*
10:15-10:45	Coffee break
10:45-11:15	Plenary discussion
11:15-12:35	Break up into groups to discuss knowledge gaps, by thematic area as follows: • Epidemiology and risk factors • Laboratory diagnosis • Supply chains and behavioural studies
12:35-13:45	Lunch
13:45-14:00	Collect results from group discussion
14:00-14:30	Plenary debriefing from group discussions *(15 min. each)*
14:30-15:00	Q&A, wrap up of knowledge gaps, plenary discussion, agreement on final statements
15:00-15:20	Mapping of ongoing and planned activities of participating institutions
15:20-15:30	Plenary session
15:30-16:00	Coffee, networking + review/completion of mapping exercise
16:20-17:20	Q&A and open discussion on opportunities for collaboration: • Field surveillance • Behavioural studies • Capacity building, training • Test development and validation • Laboratory research • Other
17:20-18:00	Wrap-up
18:30-20:00	Poster session and aperitivo

22 January Friday

09:00-09:15	**Recap of activities from day 1 and moving forward**
09:15-10:45	Presentation of One Health implementation approach under Emerging Pandemic Threats Programme Phase 2 (EPT-2), by thematic area as follows: • Surveillance and risk factors *(20 min. ppt + 10 min. discussion)* • Laboratory diagnosis *(20 min. ppt + 10 min. discussion)* • Supply chains and behavioural studies *(20 min. ppt + 10 min. discussion)*
10:45-11:15	**Coffee Break**
11:15-12:15	Facilitated discussion on cross-cutting collaboration: • Stakeholder participation • Information sharing • Communication: awareness raising, disseminating information, and risk communication • Capacity development
12:15-12:45	Implementation approach wrap-up
12:45-13:45	**Lunch**
13:45-14:30	**Coffee over topic discussions**
14:30-16:00	Collaboration building and way forward (3 pillars: surveillance and risk factors, laboratory diagnosis, supply chains and behavioural studies): • Technical • Institutional • Stakeholder Level
16:00-16:00	**Coffee Break**
16:30-17:00	Recommendations
17:00	**Closure**

USAID
FROM THE AMERICAN PEOPLE

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Annex 2
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