

Monkeypox

Current status in West and Central Africa

Report of a WHO Informal Consultation

Geneva, Switzerland, 3 November 2017



**World Health
Organization**

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EXECUTIVE SUMMARY

Monkeypox is an emerging viral zoonosis with symptoms similar to those observed in smallpox patients, although less severe. Since the global eradication of smallpox in 1980, monkeypox has emerged as the most important orthopoxvirus in humans. The Advisory Committee on Variola Virus Research (ACVVR) which meets annually to oversee smallpox research has highlighted the importance of diagnostics that could distinguish between variola and other strains of orthopoxviruses, including monkeypox virus. The ACVVR encourages the positive effects of current smallpox research on all orthopoxviruses, specifically monkeypox, such as the development of diagnostic tools.

On 3 November 2017, WHO hosted an informal consultation on monkeypox in Geneva which brought together Ministries of Health of affected West and Central African countries, AFRO and country office staff, global health partners and orthopoxvirus experts to discuss the current situation, state of knowledge, identify needs and address critical gaps and challenges in combatting monkeypox outbreaks.

Through the course of the one-day monkeypox meeting a variety of next steps were agreed upon. It was decided that a follow-up monkeypox meeting will be convened in 2018 in the African region. The meeting will include a training workshop on a newly updated monkeypox field manual to ensure district surveillance officers, laboratory technicians and clinicians have the necessary tools and are adequately trained to collect samples and manage cases. The monkeypox field manual will be developed in collaboration between WHO, CDC and Ministries of Health in the endemic countries and will include practical guidance on surveillance, case definitions, data and reporting requirements; sample collection, storage and transport; clinical case management, the use of personal protective equipment, risk communications, messaging and preventive actions, and overall disease outbreak and response guidance.

The importance of cross-border collaboration along with a one-health approach to disease management and response was highlighted. Research needs to be conducted on a number of topics in order to improve the knowledge base including understanding the animal reservoir and ecology of the disease, disease dynamics, and natural history of disease. In addition, vaccination and therapeutics require further research to enhance their application for public health interventions. Of utmost critical importance is the strengthening of laboratory capacity to identify and detect monkeypox and other orthopoxviruses within endemic countries and the region as a whole. Finally, only with improved surveillance, clinical detection, and case management capacities can there be effective control of further spread and emergence of monkeypox.

BACKGROUND

Monkeypox is a re-emerging zoonotic infectious disease which appears to be becoming more entrenched and widespread in regions where it has not been detected for decades. The virus was first identified as a naturally-occurring agent of human disease in 1970 in the Democratic Republic of Congo (DRC, formerly Zaire), and was subsequently documented in other countries of West and Central Africa. With the eradication of smallpox and subsequent cessation of routine smallpox vaccination in 1980, human monkeypox was extensively studied in DRC and was found to be a zoonotic virus (unlike variola virus which causes smallpox) with the ability for limited transmission from human to humans.

During the last five decades the majority of human infections have been reported from DRC where it is a reportable disease and now more than a thousand cases are reported annually. Prior to 2000, reports of human monkeypox outside of DRC were sparse—with 21 cases reported from 7 countries in West and Central Africa – most reported in the 1970's and 1980's. Since 2016, confirmed human monkeypox cases have been reported from Central African Republic, DRC, Liberia, Nigeria, Sierra Leone, and Republic of Congo. Many of these countries have not reported cases previously for several decades. Nigeria is currently facing the largest documented outbreak of West African monkeypox with 197 suspected cases and 68 confirmed cases. In addition, infections in wild and/or captive animals have also been detected in Cameroon, Cote d'Ivoire, and DRC, suggesting the risk of zoonotic transmission to humans from locally circulating virus.

The continued, intense focus of monkeypox transmission in DRC along with increasing numbers of human and animal infections in several countries in West and Central Africa, underscores the urgent need for coordination of disease prevention, detection and response efforts. Human monkeypox is often reported from highly forested areas where the populations are dependent on bushmeat as a protein source. The hunting and preparation of bushmeat are human risk factors for infection. This cultural aspect requires specific health promotion and prevention messages as well as coordination with animal health authorities. The geographic breadth of areas at risk for zoonotic transmission raises the possibility of disease importation to non-endemic but susceptible regions; this has been documented before in South Sudan with human cases attributed to viral movement from DRC. Most areas at-risk for monkeypox have under-resourced health services; many are also active sites of conflict and civil disturbance.

There are two distinct clades of the virus: West African Clade with a case fatality rate in unvaccinated individuals of less than 1% and the Central African Clade which can have a case fatality rate up to 11%. The incubation period is between 5-13 days and to date there is no licensed pathogen-specific treatment. Smallpox vaccine, as studied in the 1980s in DRC (administered 3-19 years previously) appears to be 85% protective to prevent disease acquisition in household contacts of a case.

RATIONALE

The WHO Advisory Committee on Variola Virus Research (ACVVR) that meets annually to oversee smallpox research has highlighted the importance of diagnostics that could distinguish between variola and other strains of orthopoxviruses, including monkeypox. The ACVVR encourages the positive effects of current smallpox research on all orthopoxviruses, specifically monkeypox, which remains endemic in certain parts of Africa.

WHO convened an informal consultation on 3 November 2017 in Geneva to discuss progress on and coordination of human monkeypox disease surveillance and response in West and Central Africa. Regional approaches to augmenting disease prevention and control will be discussed along with defining future research priorities and establishing laboratory capacities.

MEETING OBJECTIVES

The purpose of this meeting was to review the current status and state of knowledge of monkeypox in West and Central Africa and to discuss optimization of outbreak prevention and control strategies in order to mitigate further emergence and spread of this disease. Emphasis was placed on ongoing surveillance efforts, risk and ecological niche mapping, expansion of laboratory testing capacities, case management and disease control, and identification of research priorities.

Outcomes of the meeting included:

- Review current status of monkeypox epidemiology in affected African countries to enhance understanding among all partners and affected countries
- Discuss options for sharing of information, knowledge, resources and technical support to improve coordination among partners and affected countries
- Improve situational awareness of the geographical and epidemiological aspects of the disease and describe elements of a risk map
- Describe current and future research requirements as they related to prevention and control activities
- Develop a working roadmap to enhance prevention and response to monkeypox outbreaks

CURRENT STATUS OF MONKEYPOX DISEASE

In 2017 cases of monkeypox have been confirmed in Central African Republic, Democratic Republic of Congo, Liberia, Nigeria, Republic of Congo, and Sierra Leone. A brief overview of the epidemiological situation was provided by all countries with the exception of Sierra Leone and Liberia (who were not able to attend the meeting).

Below is a broad summary of key challenges endemic countries face – some are universal while other challenges are very specific to individual countries.

Some of the key programmatic and operational challenges in responding to the emergence of monkeypox include the following:

- Many affected countries do not have well-functioning disease surveillance systems which can hamper early detection and response
- Lack of knowledge about monkeypox in some countries, including at the national level
- Inadequate or inappropriate specimen collection and associated case information in order to confirm disease
- Animal surveillance, particularly related to wildlife (including bushmeat) is not systematically performed in affected countries
- Laboratory surveillance systems for testing and confirmation of disease is limited. Prior to 2017, regional laboratory capacity was only available at Pasteur Institute Bangui and National Institute for Biomedical Research, DRC.
- Systems for shipment of samples (domestic and international) for diagnostic testing are inadequate
- Seasonal nomadism, refugee movement and cross-border economic movement between and across borders impacts surveillance and hinders implementation of appropriate public health control measures.
- The cadre of trained public health professionals is limited and, although training schemes have started in some countries, it will take time to build sufficiently critical mass to build a robust programme of activities.
- Lack of availability of health care isolation areas and appropriate personal protective equipment in remote, rural areas where cases occur
- Stigmatization of monkeypox patients results in patients refusing to seek care, to be isolated and even escaping from health centres.
- Cost of care at health clinics, lack of specific treatments, and fear about the outcome are also deterrents to seeking health care
- Countries rely heavily on NGOs or polio programme team members for ad hoc surveillance and response which results in irregular activities
- Geographic access to areas where monkeypox cases occur can be difficult which hampers investigations and implementation of interventions
- Civil conflict and insecurity has hampered responses

DISEASE CONTROL AND OUTBREAK RESPONSE

Participants detailed numerous challenges related to disease control and outbreak response for monkeypox in West and Central Africa with specific focus on the following major areas: (1) clinical and case management; (2) laboratory testing and diagnostics; and (3) epidemiology and surveillance. Many of the operational challenges highlighted by countries were further elaborated on with an emphasis being placed on identifying solutions and a way forward.

Epidemiology and surveillance challenges

- Monkeypox is not systematically incorporated into the Integrated Disease Surveillance and Response system (IDSR) in most affected countries.
- Monkeypox surveillance is not done systematically and relevant data are not appropriately collected and reported across all endemic countries.
- Data management and historical record keeping of case investigation forms from monkeypox cases is limited which hinders risk and exposure assessment for interventions.
- When alerts are sent to the national level, response measures are not always undertaken because of limited resources.
- Case definitions are not standardized and training of health care workers is inadequate in most affected countries.
- There is a lack of knowledge regarding monkeypox in many endemic countries
- Specimens may not be collected or inappropriate specimens are collected, hampering the ability to confirm cases
- Animal surveillance is limited to research projects often due to lack of funding. Results from research are not systematically reported to government authorities for incorporation into prevention and control programmes such as risk communication.
- Alerting neighboring countries of confirmed monkeypox cases does not systematically occur and depends on personal relationships.

Epidemiology and surveillance recommendations

- In collaboration with all endemic countries, develop a monkeypox field manual and toolkit to aid in the development of a set of activities for a monkeypox disease control, and prevention programme.
- Ensure associated training for all endemic countries to include clinicians, laboratorians, surveillance officers for a comprehensive programmatic approach.
- Promote the inclusion of monkeypox into IDSR in countries in the endemic zone with provision of commensurate training.
- Strengthen data management, analysis and sharing functions within countries particularly for all zoonotic infectious diseases occurring within a country
- Formalize and strengthen human and animal health relationships, coordination and information exchange related to monkeypox within each of the endemic countries and the region as a whole.
- Develop a mechanism for sharing of data of animal and human monkeypox cases and develop appropriate messages for intervention and prevention.
- Build mechanisms for cross border movement communication and information sharing on confirmed cases to ensure operational readiness plans are enacted
- Strengthen One-Health approach to investigations of monkeypox cases
- Support each endemic country to have a monkeypox disease control and outbreak response plan.

Clinical challenges

- Nosocomial transmission still occurs in care settings and the standard of care is not well defined.
- Difficult for clinicians to differentiate between varicella and monkeypox presentations.
- Clinicians have difficulty monitoring clinical status of severe patients without basic clinical laboratory tests.
- Pain management and nutritional support is important yet challenging as the lesions keep patients from eating and/or drinking leading to further nutritional insufficiencies.
- The nature of person-to-person contact leading to transmission needs to be studied; some suspect sexual transmission may be one route.
- Patients suffer from stigma in their communities which hampers healthcare and response efforts as patients avoid and evade health services.
- Clear understanding of clinical presentation for clinicians for them to be able to distinguish monkeypox from the other rash illness leading to better treatment and outcome.
- Natural history of the disease course and range of symptoms are not well defined for which observational studies are needed.
- Currently there is no effective pathogen-specific therapy but supportive care targeted at signs of diseases (airway support, skincare, etc.) is of benefit.
- Psychosocial support for the patients and family as well as communication guidance is needed as part of patient management.

Clinical Recommendations

- Develop a standard data collection form for the clinical management of patients and to aid with better documentation and understanding of the natural history of disease.
- Strengthen clinician awareness of monkeypox and differential diagnosis through training including completing investigation forms and obtaining appropriate specimens for testing.
- Enhance capacities for infection prevention and control (IPC) and limit nosocomial transmission.
- Strengthen clinical laboratory capacity for supportive treatment of cases.
- Conduct operational research to better understand prognostic factors determining severity of illness.
- Evaluate investigational agents as pathogen-specific treatments such as those under the smallpox research agenda.

Laboratory challenges

- Health care workers often collect blood specimens from patients because it is the most common sample collected but for monkeypox blood can be inconclusive and it is lesion that samples allow the best likelihood of diagnosis.
- Most laboratories, even at the national level, have difficulty maintaining appropriate stocks of reagents, because of lack of funds and security conditions in some areas.

- Besides appropriateness of samples collected, timely receipt of specimens is necessary otherwise there is negative impact on quality.
- Case report forms with MPX-specific case data must be included with specimens to ensure appropriate interpretation of results (dates of illness onset, sample collection date, type of sample etc).
- GeneXpert machines can be used to test for monkeypox; however, not all countries have extra GeneXperts available for use and the cartridges are too costly for routine use in resource-poor settings
- No formal agreements exist between the affected countries in region for samples transport, particularly across borders for testing.

Laboratory Recommendations

- The most important issue is to ensure health workers collect lesion samples rather than blood from suspected monkeypox cases for appropriate laboratory diagnosis, accompanied by a core set of elements in the accompanying reporting form.
- Laboratory should be better integrated into the architecture of surveillance (e.g. through the IDSR framework) for monkeypox so detection and confirmation of cases is done rapidly.
- An inventory of laboratory locations and capacities, both in endemic countries and regionally, is necessary as a first step for developing a laboratory network.
- Development of formal mechanisms including resources for logistics and transport of samples within and among countries for laboratory diagnostics.
- Strengthen international shipment and funding mechanisms to ensure laboratory confirmation at referral laboratories for orthopoxviruses
- Create or designate reference laboratories; ensure they conduct and pass routine proficiency testing; and support the logistics of transport to the reference laboratory.
- Support use of and training for PCR and RT-PCR diagnostics capacities in endemic areas, and if possible GeneXpert machines in national laboratories.

Laboratory capacity and networks

The importance of laboratory capacity in endemic countries included discussion on how to best use orthopoxvirus laboratories for diagnostic testing of monkeypox. Understanding the Nagoya protocol and how it impacts operational work and research is important for the development of diagnostic capacities at national and regional levels. The consensus of the group was that any orthopoxvirus laboratory network focussed on monkeypox as a start should be built up gradually in incremental steps to ensure success.

Currently, country-level capacities to test for monkeypox are unclear. Recommendations were made to incorporate monkeypox into the laboratory capacity questionnaire that is administered to countries by AFRO and make this information readily available. Key issues remain:

- Although there are reference laboratories in Africa, a challenge is getting the samples to the right location in timely manner while maintaining the cold-chain.
- In order to have a successful network, the laboratories need to have samples to test and a quality control system.
- The linkage between strengthening surveillance systems and awareness of clinicians is critical in order to ensure appropriate samples are collected in the first place
- At present there is no point-of-case diagnostic or rapid diagnostic test for monkeypox that can be deployed in the field but work is underway for protein-based diagnostics that will improve field-level testing capacity. GeneXpert may be a viable option as well but currently is too expensive.

Operational and ecologic research

There are many unknowns related to monkeypox, including the animal reservoir species. A research roadmap will lead to better understanding of the animal reservoirs, the natural history of the disease, potential medical responses, and ecological niche conditions for the virus. Greater knowledge in these areas will in turn enable improved interventions for prevention and control of monkeypox.

There are several challenges in conducting operational research including the identification of control groups which are required in order to understand disease since most people who are affected reside in areas where they are in constant contact with animals. Although research has improved our understanding of how ecological changes are impacting the spread of monkeypox, there are still many unanswered questions as the distribution of the potential reservoir(s) is often misaligned with case locations. An overall risk map based on a better understanding of the ecological niche will aid in risk assessment and for implementation of prevention and preparedness measures. Population genetics and molecular epidemiology techniques are important for defining the distribution of animal reservoirs as is inclusion of climatic and geographic factors to model host hotspots. Expertise in applied veterinary sciences to make such zoonotic and ecologic studies is lacking but should be addressed through One Health schemes.

A critical area of work is for raising awareness and promoting less risky behaviours in endemic areas. Risk communication and behaviour change will need specific attention with anthropological approaches and community engagement as key components.

Medical countermeasures have been developed for smallpox that can be extended to other orthopoxviruses but none are licenced for use for monkeypox at the present time. Newer generation vaccines are in development for smallpox and have less known side effects than earlier generations. CDC is currently working with Ministry of Health and Kinshasa School of Public Health in the Democratic Republic of Congo to conduct a prospective cohort study to understand vaccine effectiveness of these newer smallpox vaccines among 1000 healthcare workers against monkeypox infections. Results are expected in 2019.

Research questions on monkeypox include some of the following:

- Which groups are most vulnerable and/or at highest risk and what is the true burden of disease in various groups?
- Is the increasing number of cases because of waning smallpox immunity or are there other factors such as ecological issues or virus evolution and virulence?
- Is the increase in case frequency a result of surveillance systems being strengthened ?
- What are the wild animal reservoirs and how does the endemic population interact with them? Are there ecological changes which are impacting the spread of disease?
- What are other modes transmission and are there asymptomatic cases?
- Is the virus sexually transmitted? Additional body fluids associated with transmission?
- What are the long term complications associated with monkeypox illness?
- What factors drive virus evolution and how is it changing over time?
- Conduct operational research on critical issues such as to better understand prognostic factors determining severity of illness and effective disease management strategies.
- Evaluate investigational agents as pathogen-specific treatments
- Evaluate disease prevention strategies to include vaccines

SUMMARY AND CONCLUSIONS

Given the array of challenges identified, it was acknowledged by the participants that much work is needed to implement a comprehensive programme of work to prevent emergence and spread of monkeypox and to control further cases in endemic areas of West and Central Africa.

The discussions during this consultation have highlighted some priority areas of work for support to countries where monkeypox is spreading and partners have all committed to bringing their comparative advantages to bear in this endeavour. Some of the next steps and actions that have been identified are as follows:

1. To develop a comprehensive field manual toolkit for use in countries with monkeypox cases which will include, but not be limited to, guidance on:
 - a. Human surveillance: case definitions, data collection, samples etc aligned with IDSR
 - b. Laboratory: diagnostics, sample transport, reference labs etc
 - c. Clinical case management: health care facility needs, supportive care, IPC
 - d. Prevention (risk communication)
 - e. Treatment measures including psychosocial support
 - f. Reservoir and animal (wildlife) surveillance aligned with One Health
 - g. Outbreak response and control (SOPs, PPE, isolation, IPC)
 - h. Research and data requirements

2. To organize a multi-country training workshop in AFRO for endemic country staff based on the toolkit in the coming year that would help establish regular activities.
3. To engage with veterinary sector through One Health, FAO, OIE and work towards building cross-border collaborations.
4. To initiate a laboratory network structure to provide necessary support for endemic countries and build capacity in diagnostics and referral testing/confirmation for monkeypox cases.
5. Facilitated by WHO, partners and global experts to continue to support countries in prevention, case detection, research and laboratory support, as needed.

Advocacy is required for mobilization of human, technical and financial resources to build a comprehensive monkeypox programme within the IDSR and One Health disease control systems.

ANNEX 1

WHO Informal Consultation on Monkeypox

Geneva, Switzerland, 3 November 2017

PROVISIONAL AGENDA

Sessions	Topic	Presenter/Facilitators
Chaired by WHO HQ		
08:30-09:00	Registration	
09:00-09:15	Welcome and introductions	WHO – Asheena Khalakdina
09:15-09:30	Monkeypox- Intro to the virus and the disease	CDC – Victoria Olson
09:30-09:45	Monkeypox in Central African Republic	WHO – Thomas D'aquin Koyazegbe & MoH – Raphaël Mbailao
09:45-10:00	Monkeypox in Republic of Congo Brazzaville	WHO – Fatoumata Binta T Diallo
10:00-10:15	Monkeypox in Nigeria	WHO – Ibrahim Mamadu & NCDC – Adesola Felicia Yinka-Ogunleye
10:15-10:30	Monkeypox in Democratic Republic of Congo	TBD
10:30-11:00	DISCUSSION –Monkeypox in West and Central Africa	Chair: WHO –Mamoudou Harouna Djingarey
11:00-11:15	Coffee Break	
OUTBREAK RESPONSE		
11:15-11:30	Clinical challenges in monkeypox outbreaks	MSF – Michel Van Herp
11:30-11:45	Laboratory challenges for monkeypox diagnostics in endemic countries	IP CAR – Emmanuel Rivalyn Nakoune Yanndoko & IP Dakar – Aissatou Toure
11:45-12:00	Challenges in epidemiology and surveillance	CDC – Andrea McCollum
12:00- 12:15	Special issues with outbreaks in conflict/migrant areas	UNHCR – Ann Burton
12:15 – 13:00	DISCUSSION – Roadmap for future response including coordination and capacity building	Chair: Mamoudou Harouna Djingarey
13:00-14:00	Lunch	

OPERATIONAL RESEARCH		
14:00-14:30	Ecology and risk mapping	CDC – Yoshi Nakazawa
14:30-14:45	Information and data sharing	WHO – Kara Durski & Jason Mcknight
14:45-15:00	Development of medical countermeasures	CDC – Brett Petersen
15:00-15:30	DISCUSSION – Further research needs	Chair: CDC – Andrea McCollum
15:30-15:45	Coffee Break	
LABORATORY CAPACITY AND NETWORK		
15:45-16:15	Proposed outline of laboratory network and summary of diagnostic capacity and needs	RKI – Andreas Nitsche & WHO – Dhamari Naidoo
16:15-17:00	DISCUSSION - Development of laboratory capacities	Chair: Dhamari Naidoo
CLOSING		
17:00-17:30	Conclusions and next steps	Participants
17:30	Closing remarks	Asheena Khalakdina

ANNEX 2

WHO Informal Consultation on Monkeypox

Geneva, Switzerland, 3 November 2017

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