Daniel Bausch, MD, MPH
Director, Emerging Threats and Global Health Security

MONKEYPOX: DIAGNOSTICS, PIPELINES, AND RESEARCH NEEDS

2 JUNE 2022
LABORATORY METHODS FOR MONKEYPOX VIRUS DETECTION

- Direct virus demonstration/isolation
- Molecular methods for nucleic acid detection
- Immunological methods for antibody or antibody detection
# DIRECT VIRUS DEMONSTRATION/ISOLATION

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<tr>
<th>Test</th>
<th>Description</th>
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<tr>
<td>Virus culture/isolation</td>
<td>Live virus is grown and characterized from a patient specimen</td>
<td>Requires a BSL-3 laboratory</td>
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<td>Electron microscopy</td>
<td>Clear image of a brick-shaped particle for visual indication of a pox virus</td>
<td>OPXV species cannot be differentiated morphologically</td>
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<tr>
<td>Immunohistochemistry</td>
<td>Tests for the presence of OPXV-specific antigens</td>
<td>Can be used to identify antigens in biopsy samples (in the absence of previous exposure to OPXVs)</td>
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# MOLECULAR METHODS FOR NUCLEIC ACID DETECTION

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<td>PCR (real-time or conventional)</td>
<td>Tests for the presence of OPVX or MPXV-specific DNA</td>
<td>Preferred method for routine diagnosis. Can allow distinction of Congo Basin and West African clades. Positive OPXV PCR is considered sufficient for laboratory confirmation of suspected cases in non-endemic countries.</td>
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<td>Sequencing</td>
<td>Gold standard for full characterization of MPXV and other OPVXs</td>
<td>Expensive and requires heavy downstream data processing</td>
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<tr>
<td>Antibody ELISA</td>
<td>Tests for the presence of anti-OPXV antibodies (IgM, IgG)</td>
<td>Extensive antigenic cross-reactivity among OPXVs, so unable to distinguish previous exposure from smallpox vaccination or other OPXV infection.</td>
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<td>Useful for excluding recent OPXV infection (presence or absence of IgM and IgG). Usually requires paired samples collected ≥ 21 days apart</td>
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<tr>
<td>Antigen-based lateral flow</td>
<td>Test for MPXV or OPXV antigens</td>
<td>Sensitivity less than NAT/PCR</td>
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<td>assay (LFA)</td>
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ELISA: Enzyme-Linked Immunosorbent Assay
LFA: Lateral Flow Assay
OPXV: Orthopoxvirus
IgM: Immunoglobulin M
IgG: Immunoglobulin G
NAT/PCR: Nucleic Acid Testing/Polymerase Chain Reaction
RECOMMENDED SPECIMENS

- Skin lesion material, including swabs of lesion surface and/or exudate, roofs from more than one lesion, or lesion crusts (all preferred over blood samples since limited duration of viremia)
- Oropharyngeal swabs
- Plasma and serum for serology
- Other specimens for research use only: urine, semen, rectal/genital swabs, whole blood
FIND is now collating a searchable directory of monkeypox tests. As a non-profit organization, we have no commercial interest in any product listed here, and inclusion of a test in this directory does not imply endorsement. Third-party usage.

22 assays to date

- 16 NAT/PCR, 3 RDT, 3 IgG Ab
- One FDA 510(k), 6 CE-IVD
PRIORITIES FOR DIAGNOSTIC DEVELOPMENT

• Validation of other sample types (e.g. oral swabs, urine, paper dots) for nucleic acid detection
• Validation of ELISA for IgM and IgG
• Validation of sequencing protocols (whole genome)
• Development and validation of antigen assays, including ELISA and rapid diagnostic tests
• On site sequencing capacity for outbreaks/molecular epidemiology (e.g. Oxford Nanopore MinION)
• Biobanks and biomaterial/availability of positive controls
LABORATORY RESEARCH PRIORITIES

- Phylogenetics from current outbreak to understand transmission patterns, potential genome changes
- Infection biology and clinical evolution of distinct West and Central Africa clades – infectivity/tropism, transmissibility, pathogenicity
- Duration of immunity post-infection and vaccination
- Inter-human transmission routes and risk factors
- Treatment: Efficacy of antivirals and immunoglobulins for severe disease and post-exposure prophylaxis
- Epidemiology: Seroprevalence studies to understand burden of disease and dynamics of transmission
- Epizoology: Characterization of reservoir hosts and their habitats and risk factors for emergence/spillover, including mitigation measures
BUT NOT ALL THE CHALLENGES ARE IN THE LAB...

• Target product profiles and market shaping
• Regional manufacturing in Africa
• Equity: > 20 commercial products announced in last 2 weeks. None before that, and none available in Africa, despite >1200 cases and 58 deaths (CFR 4.8%) in the Democratic Republic of the Congo so far in 2022
THANK YOU!

Aurélie Vessière
Deputy Director,
Pandemic Threats

Devy Emperador
Senior Scientist

FIND Business Intelligence, Data Management, Pandemic Threats, Sequencing, Biobanking, and Communications Teams