Mpox Research and Innovation

Aligning Mpox Research Response with Outbreak Response Goals

Scientific conference (29-30 August 2024)

Meeting summary Day 1

29-30 August 2024

AfricaCDC Centres for Disease Control and Prevention

CEPI

NIH National Institute of Allergy and Infectious Diseases

World Health Organization

Meeting summary: Introduction

This meeting is a call to action, making sure that research initiatives directly align with and support outbreak response goals.

- Collaborative
- Countries in the driving seat
- All partners contributing

- Expected meeting outcomes: research roadmap, facilitate collaboration, outline of key steps and timelines.

Meeting summary: Epidemiology of mpox, clinical and virologic characteristics

- Epi: Mpox is stable or decreasing in ROW, but not in Africa, where it is increasing. Largest number in DRC, with active transmission, in 9 countries right now.
- Summary Clade 1 Central Africa, Clade 2: West Africa (both in Cameroon) w. 4-5% nucleotide difference. 1a: most pediatric, mostly zoonotic driven, highest mortality 1b, 2b: most sexual transmission, 1b recent spread to Burundi, 2b Lineage A also high mortality (esp. with HIV)
- Knowledge gaps:
  - Incomplete data: increase testing including for other pathogens, including sequencing to distinguish confirmed/suspected cases. Will require deployable tests with community at center of response.
  - Address the unknowns for zoonotic Clade 1a disease, including research to find animal reservoirs.
  - Transmission dynamics: Need attack rates, incubation periods in Africa. Role of a-/pre-symptomatic transmission. More data on potential respiratory transmission.
  - Clinical presentations for the diverse clades including complications such as ocular presentations
  - Clade-associated differences in epidemiology, host factors (e..g, HIV) and transmission dynamics.
  - Immune responses & population immunity.
  - Behavioral studies.

Meeting summary: Vaccine knowledge gaps

- SAGE rec: vaccinate people at high risk of exposure; choice of vaccine based on potential risks in vaccinees, e.g., avoid replicating vaccine in infants, pregnancy, IC. Previous smallpox vaccination should not prevent monkeypox vaccination. Consider fractional dosing (more data needed). Processes to facilitate availability & equitable access to vaccines. Collect data. Sustainable investment in research.

- TPP describes minimal criteria (which current vaccines meet) and preferred criteria for monkeypox vaccines.

- Randomized initial deployment of limited vaccine supply provides a unique and ethical opportunity to obtain high quality evidence regarding uncertainties about vaccine efficacy. In ring vaccination setting, this entails vaccinating highest risk people. Randomized allocation of vaccination dates does not interfere with work of vaccination teams but allows trustworthy comparison of vaccinated vs. unvaccinated individuals. Case identification can be separate.

- Vaccine efficacy (and other questions regarding doses, schedules, safety) can and must be evaluated during deployment

Meeting summary: Vaccine Gaps Panel Discussion

- **effectiveness** studies, modifiers: HIV, malnutrition, other infections; Data on post-exposure efficacy. Fractional dosing, single dose efficacy. Clade-specific data
- Collection of real world **safety** data via active surveillance, using standardized definitions.
- Data to support vaccine use in **special populations** esp. where data aren't yet available e.g., peds, IC, pregnancy. Correlates of protection data to support other decisions
- Strategies: randomized deployment (e.g., 1 vs 2 doses, IM vs ID), test negative, vaccination registries to do appropriate follow-up, ring vaccination immediate vs. delayed., immunobridging
- Implementation:
  - Phase I studies should be done in Africa.
  - Use existing platforms & consortia.
  - Need for coordinated large studies, not lots of small studies (Africa is the only place to study multiple clades).

Meeting summary: Regulatory and ethics frameworks

- MVA-BN, LC16, and ACAM2000 have EUA or full MA for mpox in some jurisdictions, based on animal models & human immunogenicity. There are EUAs for intradermal administration of MVA, based on comparative immunogenicity. Studies of immunogenicity of MVA in children are underway. Post-marketing studies evaluated efficacy of MVA-BN.
- AVAREF procedures allow for efficient and stringent coordinated regulatory review.
- Panel discussion:
  - Regulators find data from deployment of products useful, and also support conduct of clinical research during deployment.
  - Different countries have different regulatory requirements and maintain final authority.
  - Cooperative/joint reviews via AVAREF improve outcomes and build trust and consistency, and there is high enthusiasm for this approach.

Meeting summary: Diagnostics

- Current state of diagnostic tests for MPXV: NAATs (PCR, sequencing) for diagnosis or antigen tests. Automated platfoms can be used. A few tests distinguish between clades. RDTs based on antigen or antibody have low sensitivity. More deployable POC tests are needed, and more data are needed for clade 1.
- Capture sequencing, microarrays/phage display can provide rapid broadly sensitive molecular and serological diagnostics in people and in other samples (e.g., wastewater). Columbia University is offering to train people to do these assays.
- GISAID collects MPXV sequences, submitter retains ownership of data and IP. Provides tools to support view of virus evolution e.g., relative frequency, phylogenetic trees, emerging variant tracking, 3D structure visualization

Meeting summary: Diagnostics panel discussion

- POC PCR-based diagnostics can and should be scaled up. Genexpert system is used in many labs. Many labs have significant capabilities including assay development. Sample prep (including potential inhibitors in VTM) is important. Antigen selection may depend on purpose (e.g., surveillance vs. vaccine evaluation).
- Existing collaborative networks could be used to increase places where tests can be done.
- Key needs:
  - test accuracy (should target essential genes and include appropriate controls and test the right samples).
  - RDTs aren't sensitive enough yet.
  - Important to also target other diseases that can be confused for mpox.