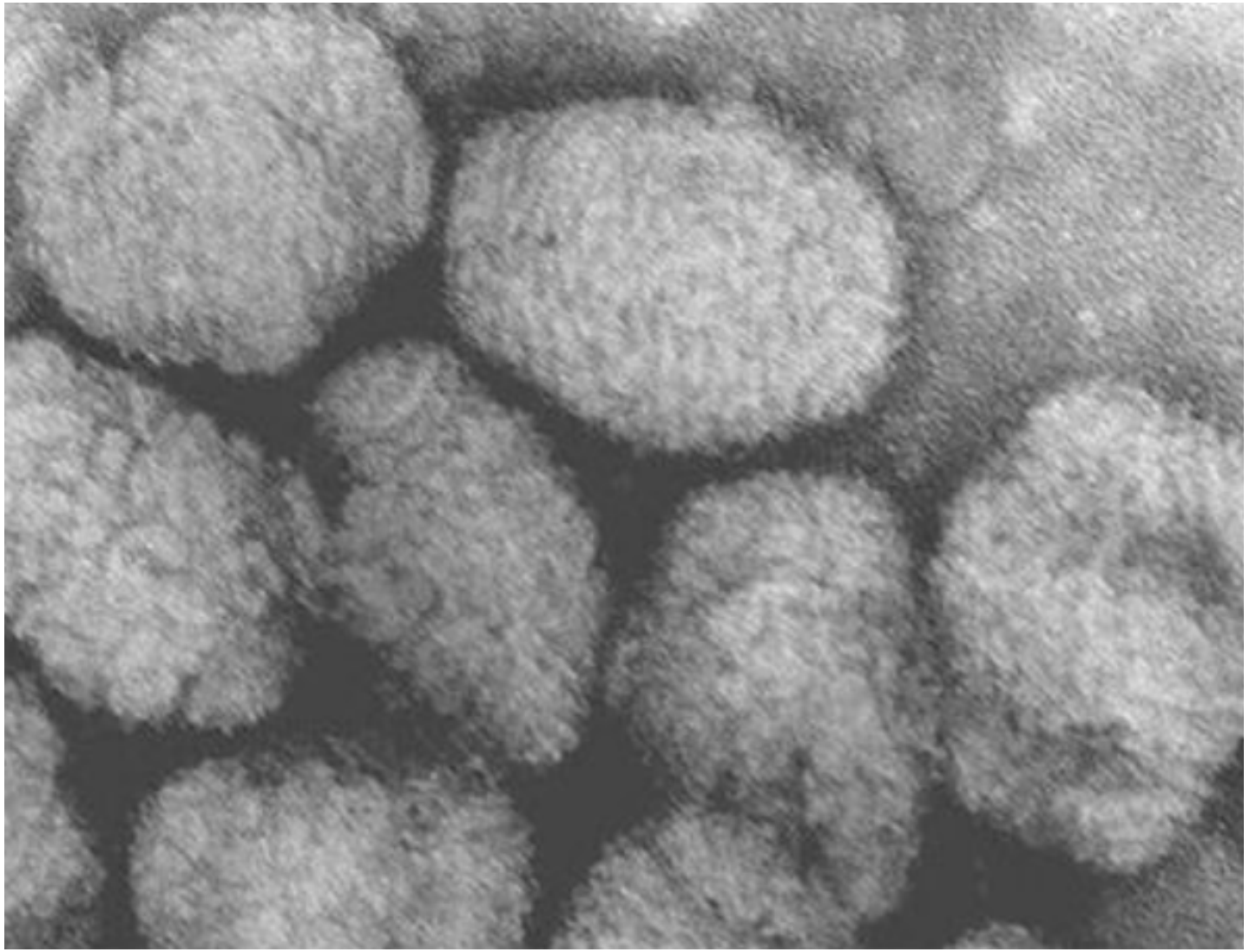
Diagnostics For Smallpox

gosh, I think we need more



John H. Connor

Boston University Chobanian and Avedisian School of Medicine

National Emerging Infectious Diseases Laboratories (NEIDL)

www.connorlab.com www.bu.edu/neidl

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Hello From The National Emerging Infectious Diseases Laboratories (NEIDL)

National Emerging Infectious Diseases Laboratories (Boston University School of Medicine)

- 1 of 2 Academic National Biocontainment Laboratories
- BSL4, BSL3, and BSL2 research facilities
- My background
  - Broad spectrum orthopox virus antiviral development
  - Diagnostic platform development with University and Biotech partners
  - Worked with hospital, private and university CLIA laboratories to provide viral genome sequencing and analysis during
    - COVID-19
    - Mpox
  - Member of the northeast Pathogen Genomic Center of Excellence (PGCoE)

I Will Comment On 3 Questions

- How has the current or most recent Mpox outbreak changed your view of the suitability or sufficiency of existing countermeasures locally, nationally, and globally?

- What are the current roadblocks to development of optimal smallpox and (other poxvirus) diagnostics/therapeutics?

- What research use cases would require live virus stock retention for research related to smallpox diagnostics and surveillance?

Components of Recent Of Effective Infectious Disease Diagnostics Responses

- Ebola virus (Ituri outbreak)
  - Automatable/multiplexable PCR-based diagnostics, multiple testing sites
  - Integration with public health and social infrastructure
  - Genomic epidemiology
- COVID-19
  - Automatable/multiplexable PCR-based diagnostics, multiple testing sites
  - Rapidly disseminated testing across govt/industry/academic sites
  - Integration with public health
  - Genomic epidemiology
- Mpox
  - Automatable/multiplexable PCR-based diagnostics, multiple testing sites
  - Integration with public health and social infrastructure

Strengths of Current Smallpox Diagnostics

- There is a CDC-developed rt-PCR assay
  - 2 targets
  - Differentiates variola from other orthopoxviruses
- Existing Biofire assays
- Why is this encouraging?
  - This is similar to diagnostics available at the start of the Mpox outbreak
    - Worldwide sharing and dissemination was helpful

Diagnostics Challenges In Responding To A Smallpox Infection Event

- Unique rules for possession of smallpox virus or viral DNA will cause immediate limitations in the response
- The diagnostic stance for smallpox continues to be in a catch-up mode
  - Biofire example (in development)
  - Strategy for expansion at viral testing sites not well established
  - Unclear whether diagnostics can be evaded through genetic change
- There are few/no alternate testing modalities
  - No point of care test (paper-based, other at-office-or-home tests)
- It is unclear whether helpful genomic epidemiology can be implemented in a timely fashion

Development of Cutting-Edge Diagnostic Response Is Hampered by Limitations on Authentic Virus

- Lack of a biobank of smallpox positive clinical specimens restricts dissemination of diagnostic approaches
- Validation of existing tests will require creation of a pseudo-specimen panel
  - Single authorized site is a bottleneck
- Creation and validation of new/advanced diagnostics will require authentic virus
  - Paper-based tests
  - LAMP
  - Optical detection
  - Electrical detection
- Implementation of genomic analysis
- Live stocks in the advent of evolved or mutated smallpox that shows altered diagnostic sensitivity

What I (and maybe only I) Think Would Make For A More Effective Diagnostic Response To Smallpox

- 2-4 target PCR-based diagnostic
  - Validated using mock-clinical samples using different DNA isolation strategies, different diagnostic platforms
- Antigen-based RDT
  - Validated on mock clinical samples using different lysis approaches
  - Anticipated use during unusual situations or high-volume infection
- Established viral genome sequencing approach
  - Validated, analysis pipelines pre-established, data sharing path known

“The eradication of smallpox occurred prior to the development of the majority of modern virological and molecular biological techniques. Therefore, there is a considerable amount that is not understood…”

Olsen and Shchelkunov

Viruses 2017 Aug 27;9(9):242. doi: 10.3390/v9090242