

Case Studies in Infection Prevention and Control of Emerging Infectious Diseases

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October 13, 2023

Orange County APIC Annual Education Conference

Disclosures

- None

Disclaimer: The findings and conclusions herein are draft and have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.

Background

- Recent examples of risk for non-Ebola viral hemorrhagic fever pathogen importation to U.S.
 - Marburg virus disease outbreaks in Equatorial Guinea, Tanzania (2023)
 - Lassa, Crimean Congo Hemorrhagic Fever are often possible diagnoses for ill returning travelers from endemic regions
 - 2 U.S. patients with Nipah on the differential diagnosis (2023)
 - Single imported Andes virus case (person-to-person transmissible hantavirus) in U.S. (2018)

Infection Prevention and Control (IPC) Guidance – Key Questions

- How is the pathogen transmitted?
 - Person-to-person
 - Contact (skin, mucous membranes)
 - Sexual
 - Air (droplets, aerosols)
 - Percutaneous (needlesticks)
- What recommendations for patient isolation and personal protective equipment (PPE) will best protect HCP and other patients from pathogen transmission?

Case Study 1: Mpox - 2022

Mpox Background

- Poxvirus related to smallpox
- Endemic to West and Central Africa
 - West African clade: milder illness
- Signs and symptoms:
 - Characteristic rash preceded by prodromal symptoms (e.g. fever, lymphadenopathy, flu-like symptoms)
- Treatment:
 - Supportive care typically enough
 - Antivirals are available through consultation with CDC
- Mortality rate: 0-11% (higher in younger children)



World Health
Organization

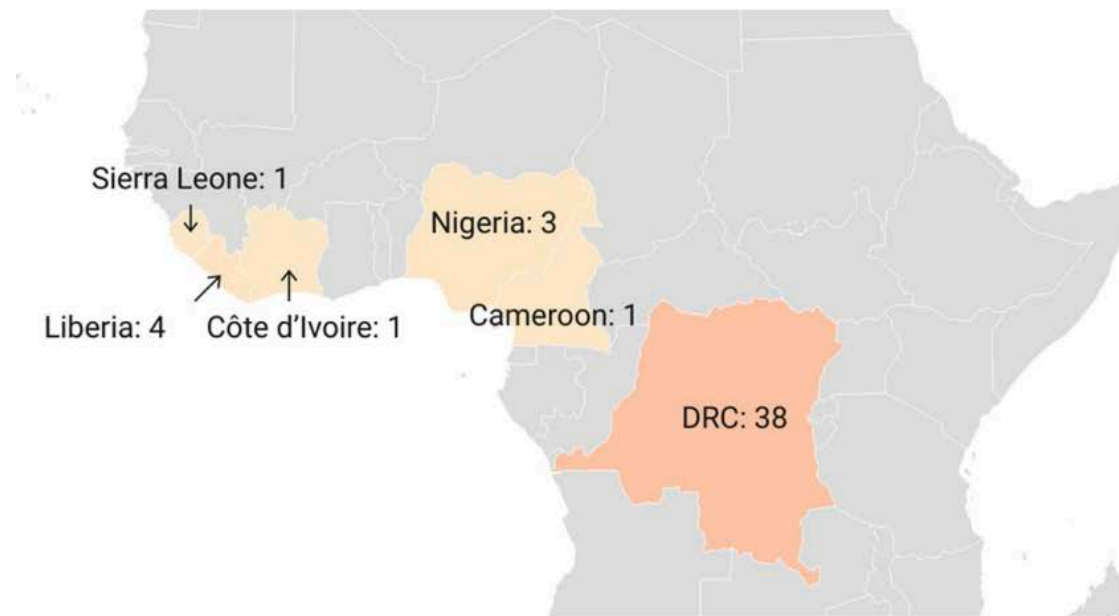


Fig 2. Number of confirmed, probable, and/or possible monkeypox cases between 1970–1979. [5,42,51] (base layer of the map: <https://datawrapper.dwcdn.net/W7k0L/4/>).

<https://doi.org/10.1371/journal.pntd.0010141.g002>



Fig 6. Number of confirmed, probable, and/or possible monkeypox cases between 2010–2019. [7,8,15,18,29,30,32,33,35,47–49,55–57,59–67,72–74] * Number reflects suspected cases, since as of the year 2000, the number of suspected cases was primarily reported by the DRC. (base layer of the map: <https://datawrapper.dwcdn.net/UUYbg/1/>).

<https://doi.org/10.1371/journal.pntd.0010141.g006>

Background

- Prior to 2018:
 - Outbreaks in endemic settings in Africa
 - Outbreak of 47 cases in US Midwest in 2003 tied to contact with exotic rodent pets → no human-to-human transmission
- From 2018 to May 2022, 9 imported cases of mpox to non-endemic countries
 - United States (2)
 - United Kingdom (5)
 - Israel (1)
 - Singapore (1)



Transmission

- Direct or indirect contact with body fluids
 - 2022 – transmission described through contact during sexual intercourse
- Contact with fomites
 - Transmission to UK healthcare worker whose only exposure was changing/shaking contaminated linens
- Exposure to respiratory secretions
- Patients infectious once symptoms begin (including prodromal symptoms) until lesions scab and scabs fall off

Examples of high and intermediate-risk exposures

- Shared towels and bedding (infectious body fluids and scabs may be present)
- Skin-to-skin contact with a patient who has mpox
- Being inside the patient's room or within 6 feet of a patient during any procedures that may create aerosols from oral secretions, skin lesions, or resuspension of dried exudates, without wearing an N95 or equivalent respirator (or higher) and eye protection
- Good news: **not easily transmitted**

Human-to-human MPX Transmission – United States, 2003

- 81 exposed HCWs to 3 patients with MPX at 2 hospitals and clinic in Indiana
- 40/57 (70%) had ≥ 1 unprotected exposure
- 1/57 had been previously vaccinated for smallpox
 - Had one encounter with MPX patient to take vital signs and physical exam – wore gloves, no direct skin contact was recalled
 - Same HCW developed anti-OPX IgM in acute- and convalescent-phase serum specimens
- 0/57 had any signs or symptoms of illness

Mpox Transmission – United Kingdom, 2018

- 3 HCWs had ≥ 1 episode of close contact with bedding/clothing of patient who would later be diagnosed with MPX
- One HCW received smallpox vaccination 5 days after most recent exposure and 6-7 days after earliest exposure
 - Developed facial lesions 8 days after vaccination
 - Only exposure risk was changing of potentially contaminated bedding
- Was virus aerosolized during changing of bed linens?

Central African Republic – 2015/2016



Figure 1. Disseminated cutaneous lesions consisting of macules, papules, and vesicles on the entire body of the primary case (case 1) (1A), on the face (1B) and legs (1C) of the mother (case 4), and rash and cervical lymph node of the hospital nurse (case 5) (1D).

Mpox – 2022

- Atypical features
 - Rash still characteristic, but often starting in genital and perianal areas
 - Rash sometimes not disseminating to other parts of body
 - Being recognized as outpatient clinics because easily confused with sexually transmitted infections
 - Prodromal symptoms mild or not occurring
- Reasons for atypical presentation not clear

What personal protective equipment should be used?

- Standard Precautions + notification of IPC personnel
- PPE to use:
 - Gown
 - Gloves
 - Eye protection
 - N95 respirator or higher

Exposures and suspected/confirmed patient management

- Monitor patients with an exposure for 21 days
- During the 21-day monitoring period, if a rash occurs, patients should:
 - Be placed on empiric isolation precautions for mpox until (1) the rash is evaluated, (2) testing is performed, if indicated, and (3) the results of testing are available and are negative.
- Those with suspected mpox infection should have recommended isolation precautions for mpox maintained until mpox infection is ruled out
- Those with confirmed mpox infection should have recommended isolation precautions for mpox maintained until all lesions have crusted, those crusts have separated, and a fresh layer of healthy skin has formed underneath

How should patients with an MPX exposure be managed?

- Correct and consistent use of PPE when caring for a patient with mpox infection is highly protective and prevents transmission to HCP
- However, unrecognized errors during the use of PPE (e.g., self-contaminating when removing contaminated PPE) may create opportunities for transmission to HCP
- Therefore, in the absence of an exposure, HCP who enter a contaminated patient room or care area while wearing recommended PPE, should be aware of the signs and symptoms of mpox
 - If any signs or symptoms of mpox occur, HCP should notify occupational health services for further evaluation and should not report to work

HCP Exposures to MPX Patients – Colorado, 2022

- May 1-July 31 2022 (3 month period)
- 313 HCP interacted with patients with subsequent diagnosed MPX
 - 23% wore all recommended PPE during their exposures
 - 28% had high- or intermediate-risk exposures and eligible for PEP
 - 48% of eligible (12% of total) received PEP
 - 0 developed MPX
- Good news – risk of transmission is low

Transmission of MPX to HCW via unknown source - CA 2022

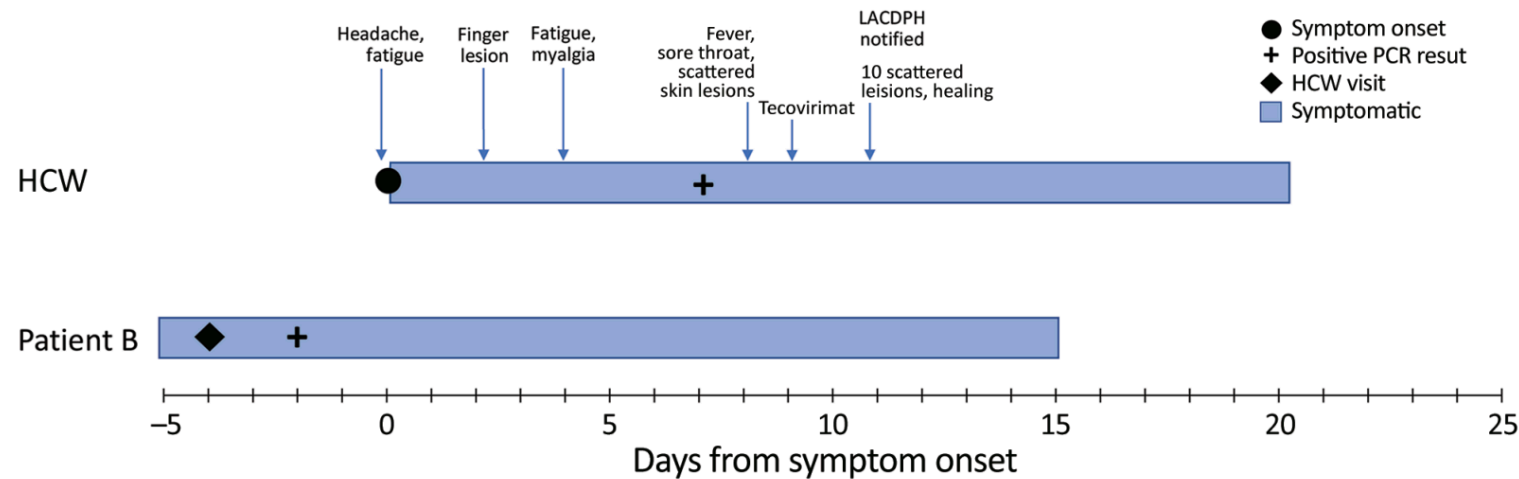


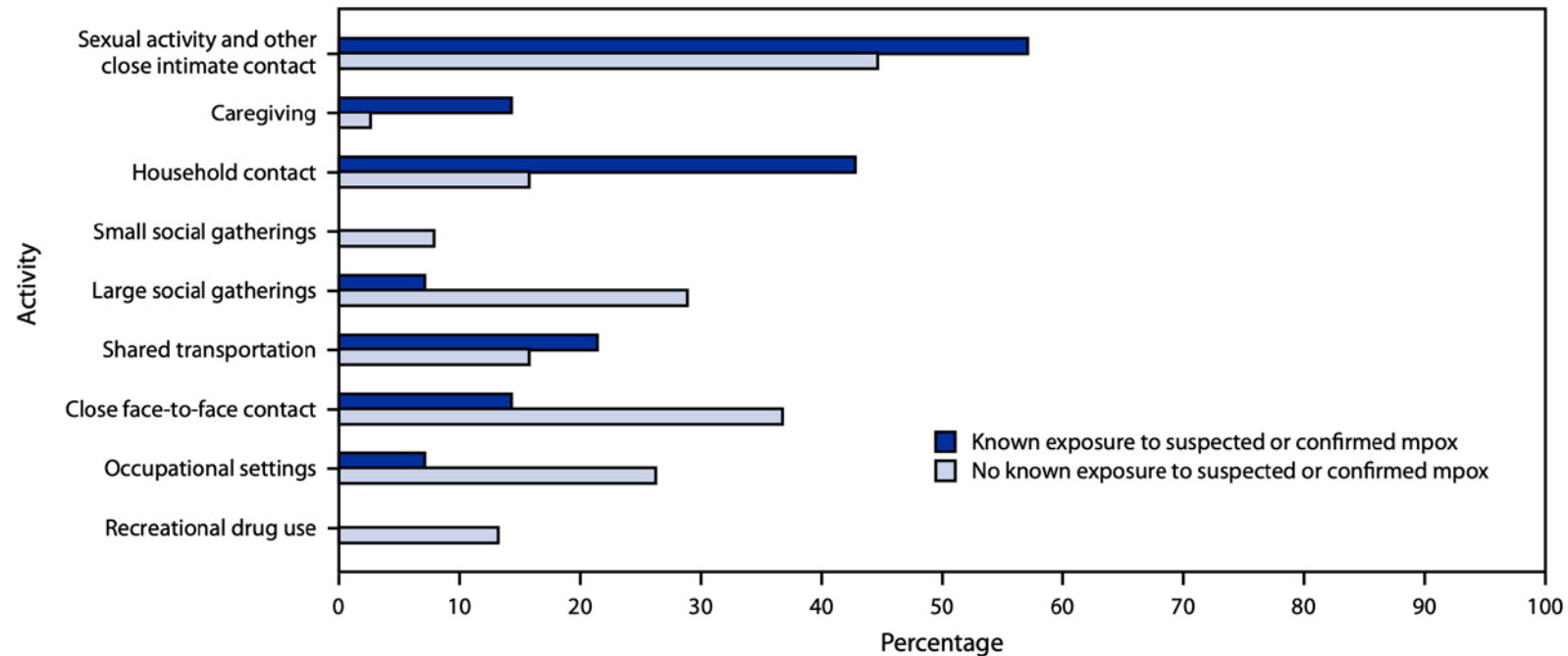
Figure 2. Timeline of symptom onset, testing, treatment, and public health interventions in response to a case of occupationally acquired mpox in an HCW, California, USA, 2022. Patients A and B were treated by the HCW during the presumed incubation period of her infection; however, course of illness for patient A is not shown because the HCW's contact with patient A was >21 days before symptom onset. HCW, healthcare worker; LACDPH, Los Angeles County (California) Department of Public Health.



Figure 1. Evolution of finger skin lesions in healthcare worker occupationally exposed to monkeypox virus, California, USA, 2022. A) August 29; B) August 31; C) September 4; D) September 5; E) September 6; F) September 7; G) September 24; H) September 28.

Unknown exposures (community)

FIGURE. Self-reported activities* of mpox patients aged ≥ 18 years who did not report male-to-male sexual contact, by known[†] or unknown[§] exposure to a person with suspected or confirmed mpox — United States, November 1–December 14, 2022

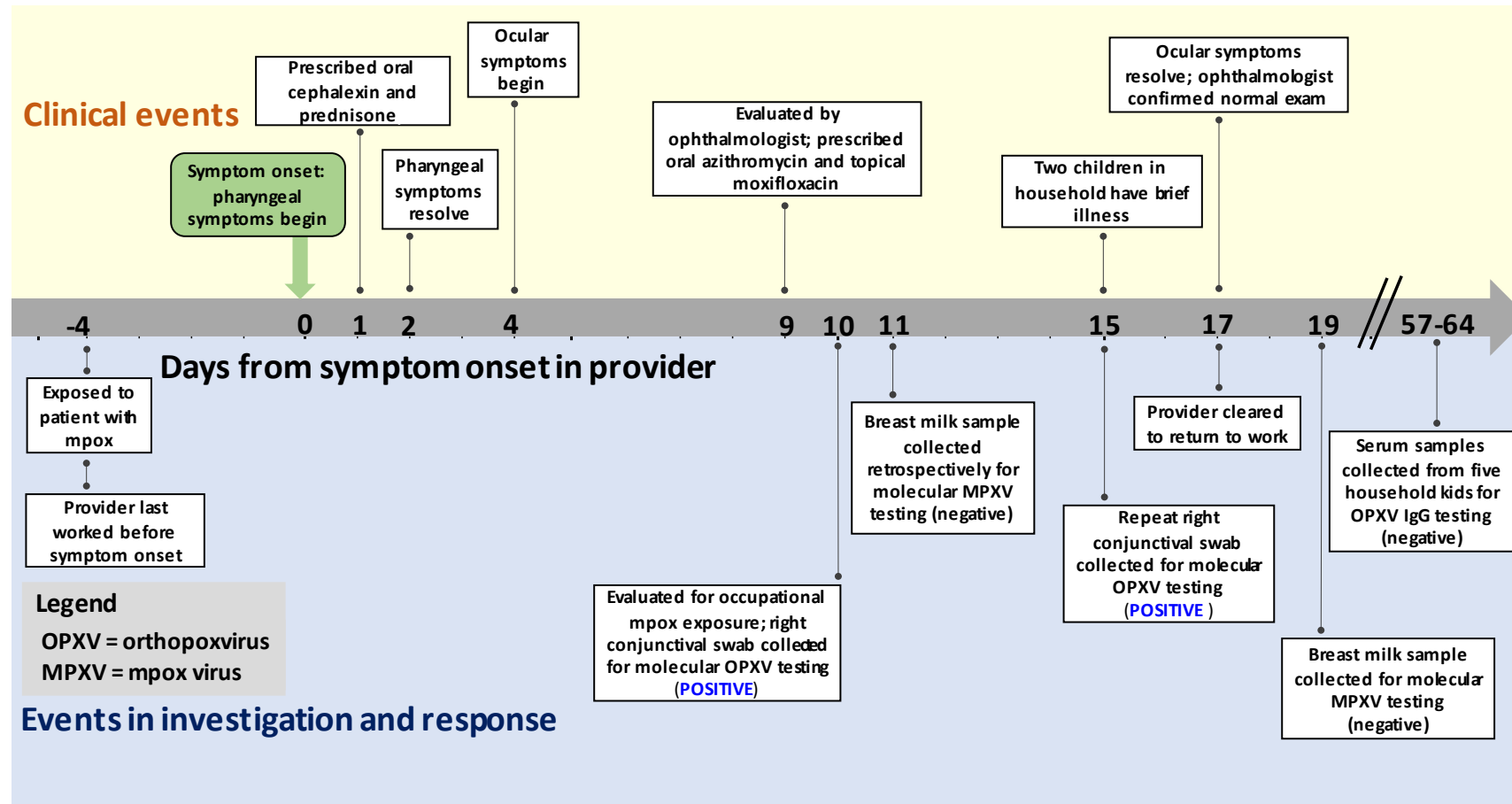


* Activities during the 3 weeks preceding symptom onset are not mutually exclusive.

[†] Percentages calculated out of 14.

[§] Percentages calculated out of 38.

Ocular mpox in a healthcare provider, 2022



Tips for Adequate Collection of a Lesion Specimen from a Suspect Monkeypox Virus Case

Vigorous swabbing of lesion specimens maximizes the probability of achieving accurate diagnostic results. **Specimens that do not contain enough human DNA may lead to inconclusive PCR test results, with no positive or negative result.** Inconclusive results necessitate patients being sampled again which can delay diagnosis. Follow the instructions below to make sure your specimens are adequate for testing. While vigorous swabbing on the surface of a lesion should collect enough viral DNA, more viral DNA can be found in crusts when present. Recommended [infection prevention and control practices](#), including the use of personal protective equipment (PPE), for caring for a patient with suspected or confirmed monkeypox infection should be used during specimen collection: [What Healthcare Professionals Should Know](#). Unroofing or aspiration of lesions (or otherwise using sharp instruments for monkeypox testing) is **not necessary, nor recommended due to the risk for sharps injury**.

Swabbing of Lesion Surface:

1. Use sterile, synthetic swabs. Do not use cotton swabs.
2. More information on specimen collection can be found here: [Preparation and Collection of Specimens](#).
3. Do not clean the lesion with ethanol or any other disinfectant prior to swabbing.
4. Hold the swab with a firm grasp. Avoid touching the swab shaft at least an inch before the tip if collecting a dry swab and the length of the swab shaft that will be submerged in liquid if using a swab to be stored in viral transport media. 
5. Apply firm pressure (generally firm enough so that the swab shaft, if plastic, may bend slightly). This may result in discomfort or slight pain, but it is necessary to obtain adequate DNA.
 - a. If lesion ruptures while swabbing, ensure that swab collects lesion fluid.
 - b. If possible, avoid using swabs that bend too easily which may make applying firm pressure difficult.
6. Swipe the swab back and forth on the lesion surface at least 2-3 times then rotate and repeat on the other side of the swab at least 2-3 times. 
 - a. If material is visible on the swab surface (such as skin material or from lesion fluid that is leaking from the lesion), this is indicative of an adequate collection. Although please note that material may not always be visible on swabs.
7. Place swab within appropriate container. 
 - a. Ensure container, storage and shipping conditions are approved by laboratory that specimen is being sent to for testing.

Collection of crusts from healing lesions:

Crusts are not accepted by all laboratories as an approved specimen type. Ensure the laboratory that will be receiving the specimen for testing is able to test crusts before collecting or sending.

1. Use a forceps or other blunt-tipped sterile instrument to remove all or a piece of the crust at least 4mm x 4mm – about the size of this dot: ● 
2. Separate each crust into a dry, sterile container. 
 - a. Ensure container, storage, and shipping conditions are approved for laboratory that specimen is being sent to for testing. 
3. Cover lesion with band aid.

IPC for Mpox – Summary

- Transmissions to HCP have occurred but are rare
 - May occur through needlestick, exposure to environment (e.g. linens)
 - Unroofing lesions for swabbing – dangerous and not recommended
- Defining risk exposure category is critical to determining need for PEP and HCP monitoring and work restrictions
- Challenges moving forward:
 - #1: Importance of HCP education re: atypical disease presentation (e.g. atypical rash appearance, location, prodromal symptoms-only)
 - #2: Importance of proper HCP donning, doffing, hand hygiene to minimize risk of self-contamination
 - #3: Delineating role of environmental contamination

Case Study 2: Nipah virus

Nipah Virus

- Family Paramyxoviridae, genus Henipavirus
- Reservoir: flying fox (aka fruit bat); *Pteropus*
- Transmission via contact with bats, consuming food products contaminated by body fluids of bats (date palm sap, partially eaten fruits)
- Close contact with infected person or their body fluids (probably resp secretions?)

Clinical Progression

- Non-specific prodromal phase (fever, HA, myalgia, dizziness)
- Neurological symptoms within 1 week
 - Coma, hyporeflexia, areflexia, segmental myoclonus, seizures
- Wide range of mortality depending on outbreak but 32-73% range
- Survivors may experience relapse (i.e. second case), or late-onset encephalitis

Nipah Virus

- First outbreak Malaysia/Singapore 1998-1999
 - 265 cases, 105 deaths
 - Pig contact
 - No human-to-human transmission identified
 - 1 possible asymptomatic case was identified much later
- Subsequent outbreaks in Bangladesh '01, '03, '04
 - Human-to-human transmission identified including nosocomial cases



***Pteropus* Bats Presence and Nipah Virus Outbreaks**

- Nipah virus infections in people
- Known or likely presence of *Pteropus* bats in the Asia, South Pacific, and Australia region

Nipah Virus - 2023

- 2 cases in US where Nipah virus arose on differential diagnosis
 - Patients had history of travel to endemic or possibly endemic areas in SE Asia
 - No other known epidemiological risk factors (e.g. contact with bats)
 - Clinical symptoms not entirely consistent – testing ultimately not requested in favor of other differential diagnoses

Healthcare Transmission – Bangladesh 2004

- Seroprevalence study and exposure survey of HCW's caring for NiV patients
 - 23% of nurses used PPE, 19% of physicians
 - 32% had unprotected exposures to body fluids (splash to eye, mouth, or nose with bodily secretion or needlestick injury)
- 0/105 HCWs IgM+, 2/105 IgG+*
 - Family members provided most of the hands-on care

TABLE. Type of Healthcare Worker Exposures to Patients With Nipah Virus Infection During January and February 2004 at Dhaka Medical College Hospital, Dhaka, Bangladesh

Type of exposure	No. (%) of healthcare workers exposed (n = 105)
Washing and changing bed sheets	52 (50)
Performing a physical examination	38 (36)
Drawing blood	35 (33)
Direct skin contact with respiratory secretions, stool, urine, or blood	30 (29)
Providing suction	27 (26)
Giving an injection	25 (24)
Placing a canula	17 (16)
Placing a nasogastric tube	11 (10)
Performing funduscopy	10 (10)
Changing bedpans	7 (7)
Receiving a needlestick injury	7 (7)
Performing lumbar puncture	6 (6)
Being splashed in the eye, nose, or mouth with respiratory secretions, stool, urine, or blood	6 (6)
Placing a catheter	2 (2)

Healthcare Transmission – Siliguri, India 2001

- Minimal use of PPE or “barrier nursing methods” by staff prior to outbreak

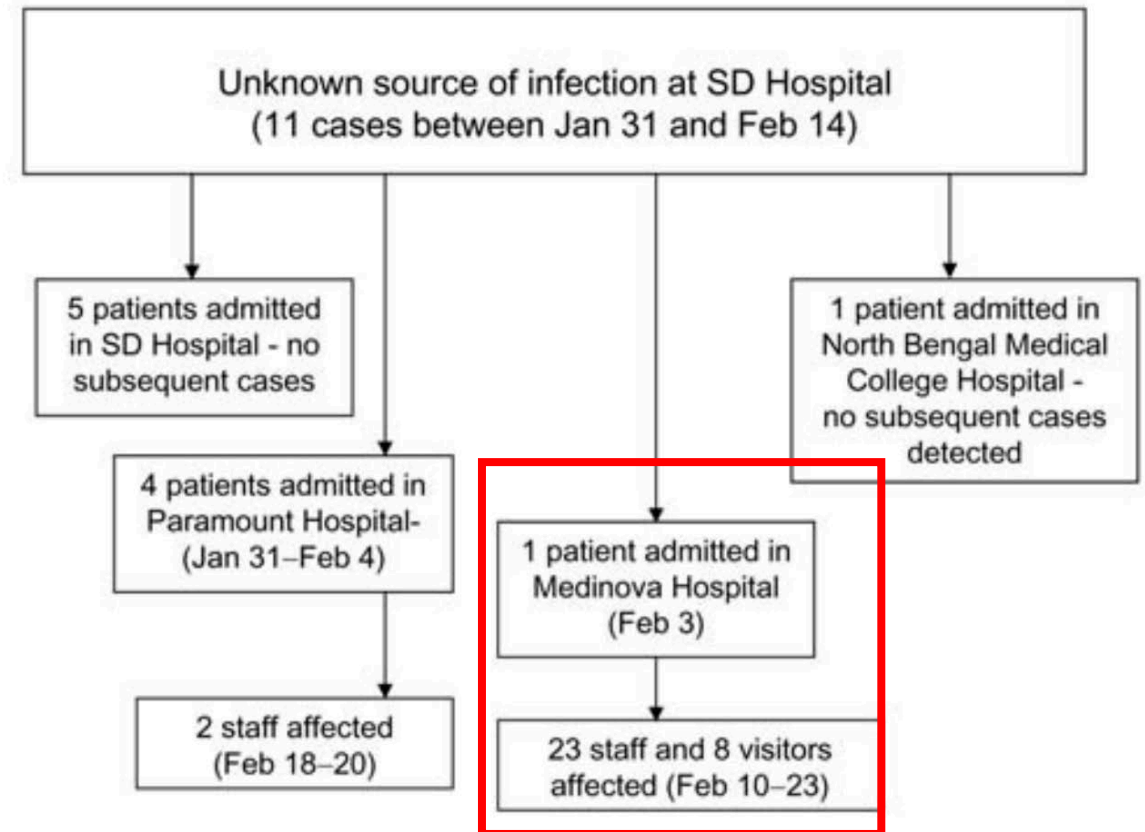


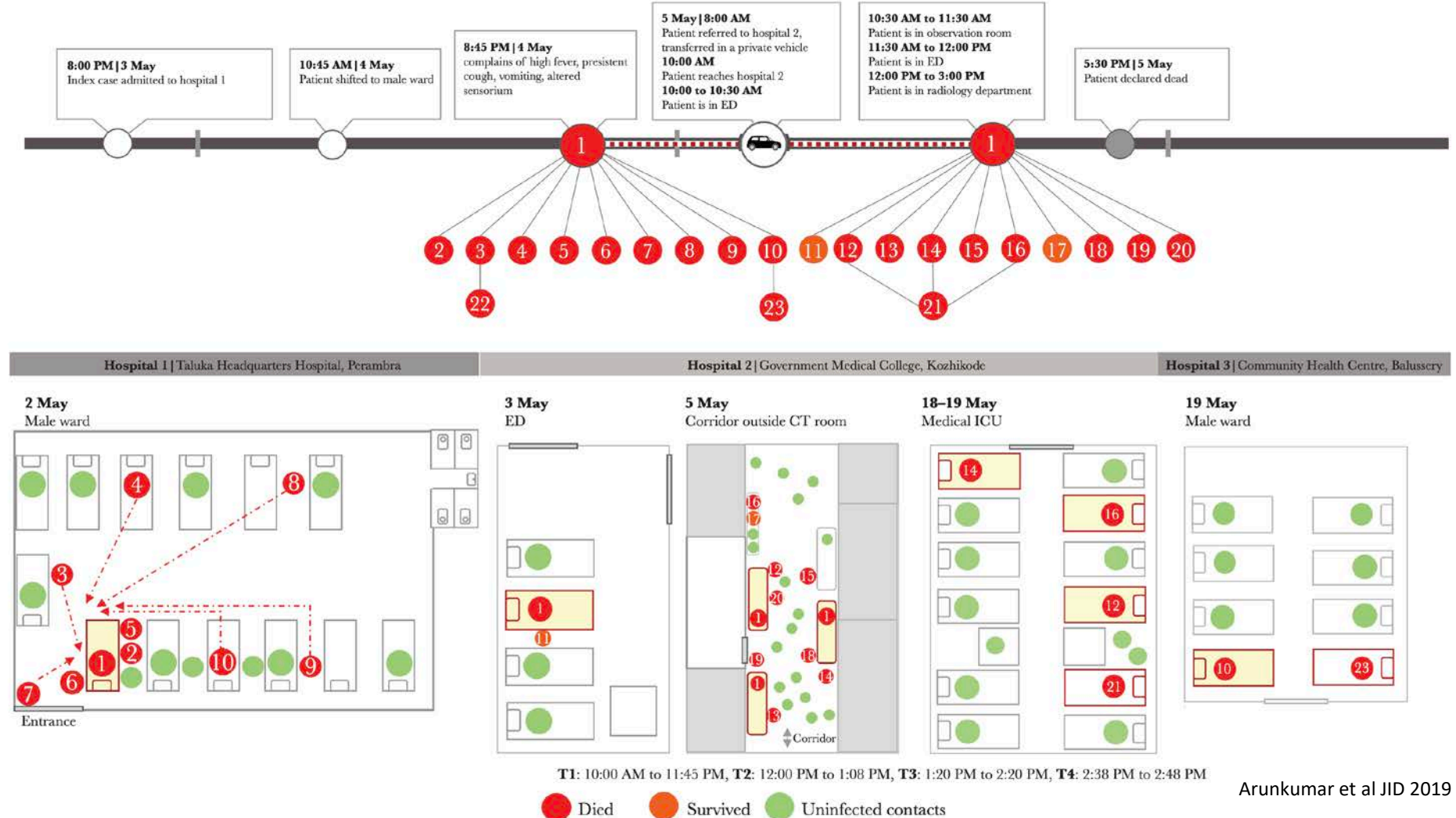
Figure 2. Sequence of events in the Siliguri (SD) outbreak.

Healthcare Transmission – Kerala, India 2018

- 23 cases – only index infected in community, rest nosocomial, including HCWs
- Index case transmitted to 19 contacts with 3 secondary cases

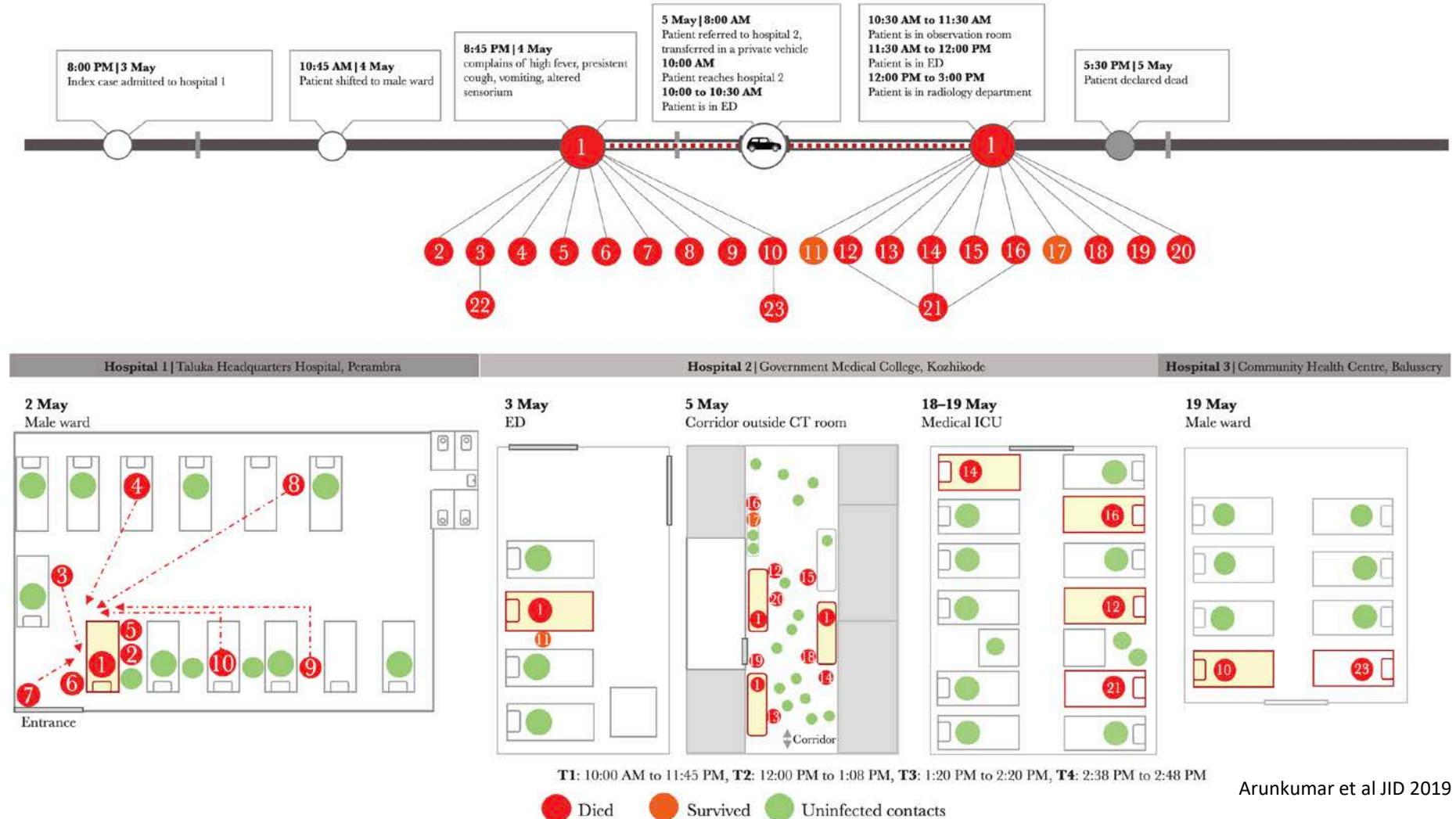
Hospital Transmission – India, 2018

- 2 = brother
- 5 = father
- 6 = aunt
- 7 = nurse
- 3,4,8,9,10 = patients/companions who helped case 1 or came close to his bed
- Mother didn't become infected (wore scarf over her face to help with hospital smell) – less contact with patients than brother/father
- Sick patients restricted to beds didn't get sick



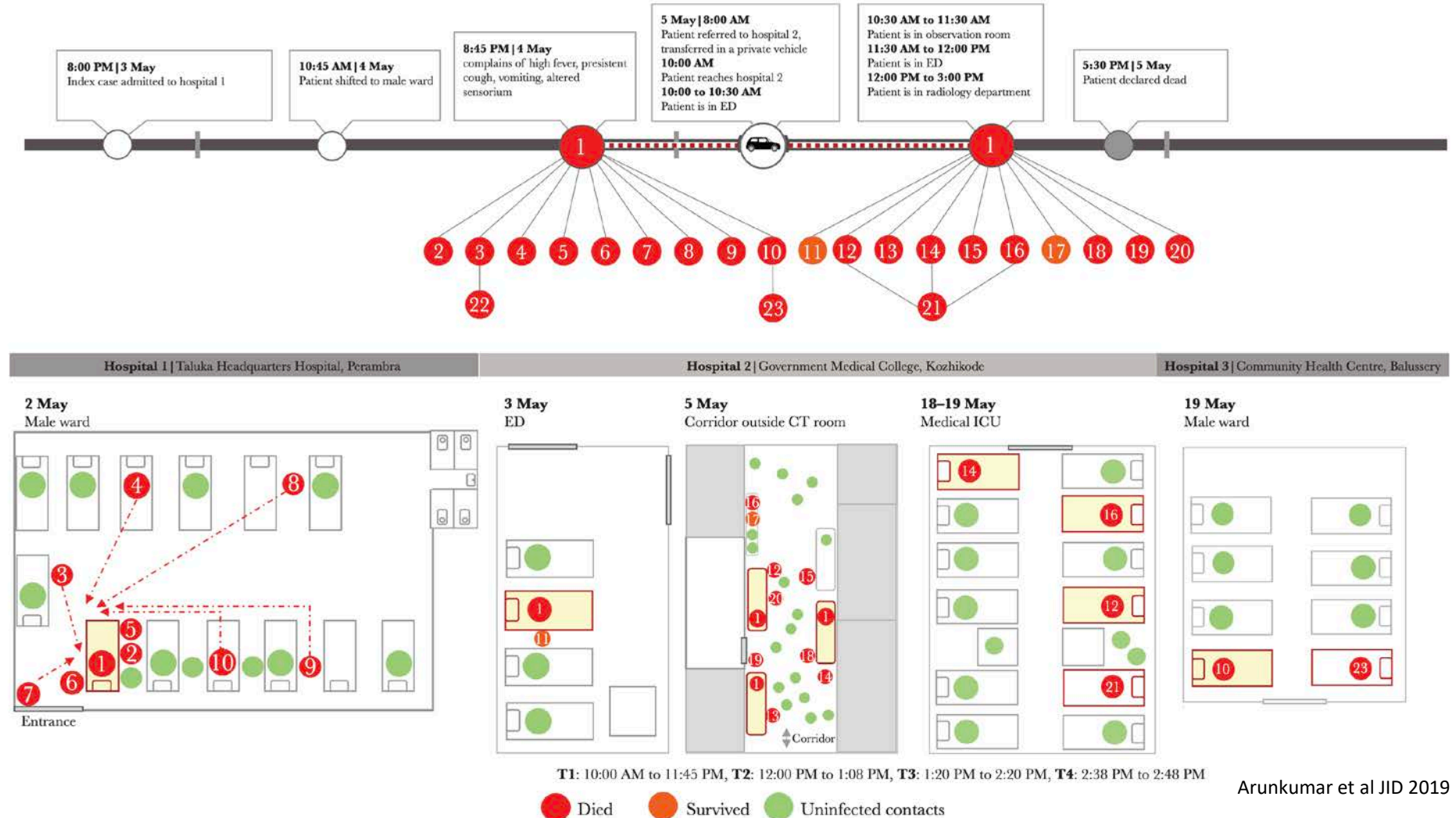
Hospital Transmission – India, 2018

- 11 = trainee who collected samples
- 12-18, 20 = present in corridor outside CT room while patient was coughing
- 19 = radiology assistant
- 70-100 total people in corridor during patient's 3 hours waiting for CT
- Most transmissions occurred within 2 days before 1's death



Hospital Transmission – India, 2018

- 10 (secondary case of 1) transmitted to 23 (bed across)

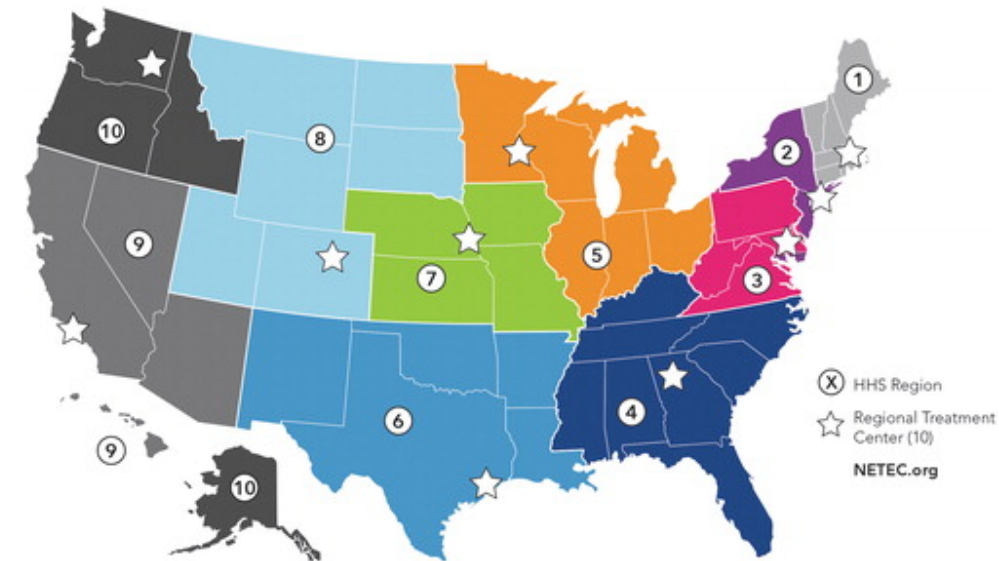


Healthcare Transmission – Kerala, India 2018

- Only a few HCWs were using “any barrier protection measures, such as a face mask and gloves”
 - “Healthcare workers or companions with adequate barrier infection control practices did not acquire NiV despite close contact with the index case” (Arunkumar et al)
- Numerous individuals touched/bathed/carried 1, 3, 4, 8, 12, and 16’s bodies but no secondary cases reported from these
 - Bangladesh 2010 – 2 patients with suspected transmission from corpse (Sazzad et al EID)
- Secondary cases all had “closer and longer contact, touched body fluids, or were coughed on”

Nipah virus Patient Placement and PPE

- Patient Placement: AIIR
- PPE:
 - *If suspect Nipah case and clinically stable*: gown, gloves, eye protection, N95 respirator or higher
 - *If suspect Nipah case and clinically unstable (e.g. hemodynamic instability, vomiting) OR confirmed Nipah case regardless of clinical stability*: use PPE according to clinically unstable VHF guidance



Regional Treatment Centers

- 1: Massachusetts General Hospital
- 2: NYC Health + Hospitals/Bellevue
- 3: Johns Hopkins Hospital
- 4: Emory University Hospital and Children's Healthcare of Atlanta – Egleston Hospital

- 5: University of Minnesota Medical Center
- 6: University of Texas Medical Branch at Galveston
- 7: University of Nebraska Medical Center
- 8: Denver Health Medical Center
- 9: Cedars-Sinai
- 10: Providence Sacred Heart Medical Center and Children's Hospital

Regional Emerging
Special Pathogen
Treatment Centers
(RESPTC)

Summary

- Nipah virus is an emerging pathogen capable of human-to-human transmission with high mortality and no vaccine/treatment
- No US cases to date
- Risk Factors for human-to-human transmission:
 - Contact with body fluids, especially respiratory secretions
 - Prolonged exposure to case-patients especially those with respiratory symptoms and older age

Summary

- Unknowns:
 - Risk of transmission in patients without respiratory symptoms
 - Risk of transmission in patients with chronic or relapsed disease (rarer)
 - Duration of transmission
- IPC Challenges:
 - Timely identification, early clinical suspicion + testing → minimize exposures
 - Prompt clinical management with HCP trained in appropriate PPE and IPC techniques
 - Duration of precautions – case-by-case basis

Case Study 3: Lassa virus

Lassa virus

- First isolated in Sierra Leone¹ during epidemic
- Lassa virus prevalence near 20% in West Africa
- Rodents are asymptotically infected and shed the virus in saliva, urine, and feces
- Humans exposed to rodent excreta may become infected
- Humans may transmit to other humans through body fluids (e.g. blood, saliva, urine, vomit) or through objects contaminated by body fluids

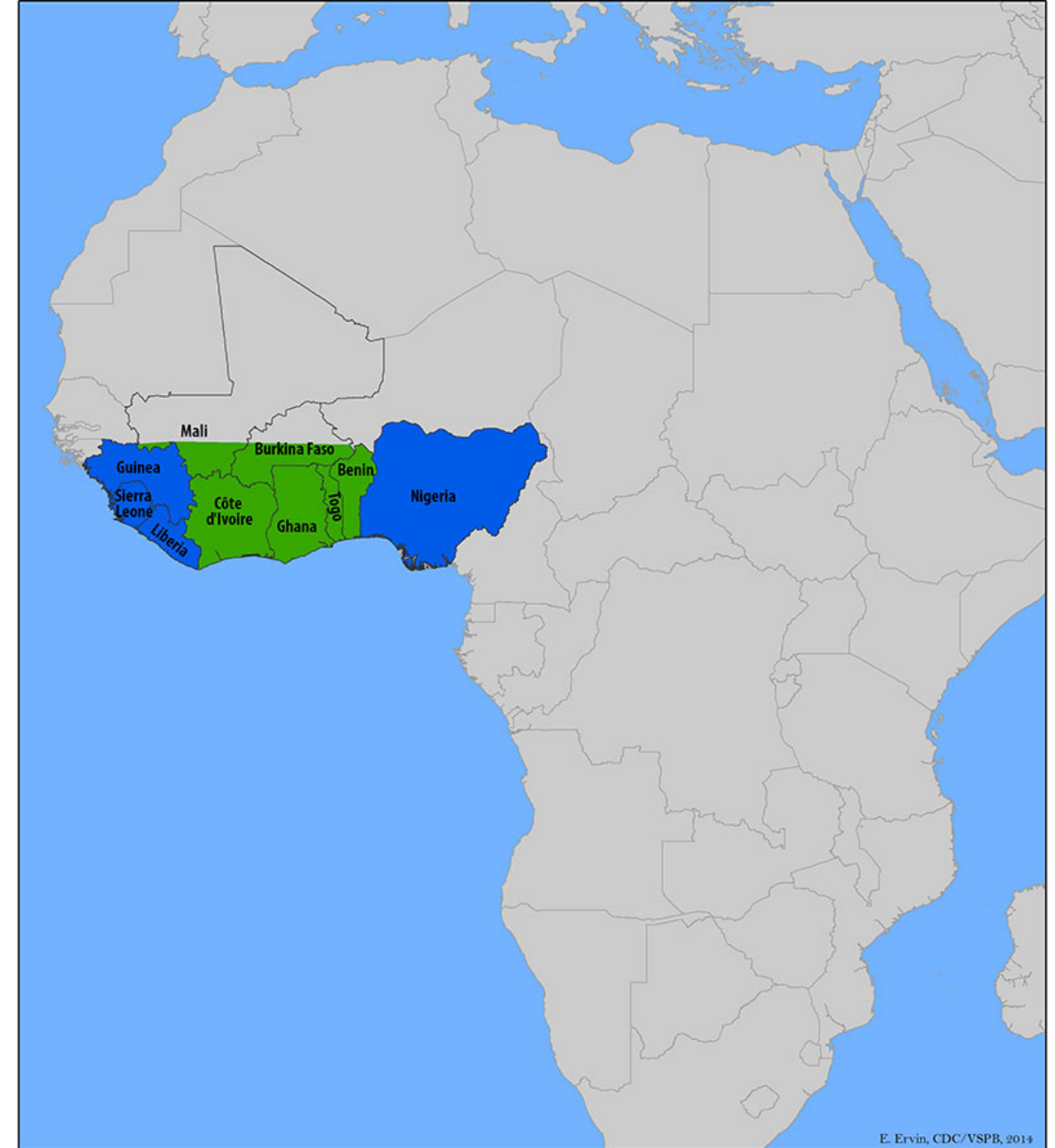


Clinical Features

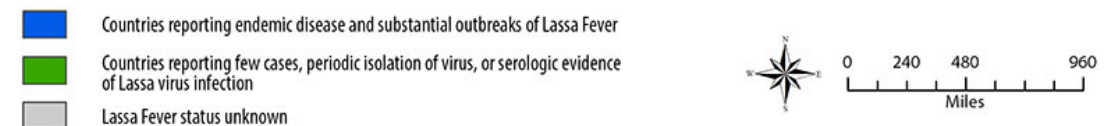
- **Mild symptoms:** flu- like illness
- **Severe symptoms:** hemorrhage, respiratory distress, vomiting, hearing loss, tremors, encephalitis, multi-organ failure

Lassa Fever

- Endemic to several countries in West Africa¹
- 100,000-300,000 annual cases
- 5,000 annual deaths

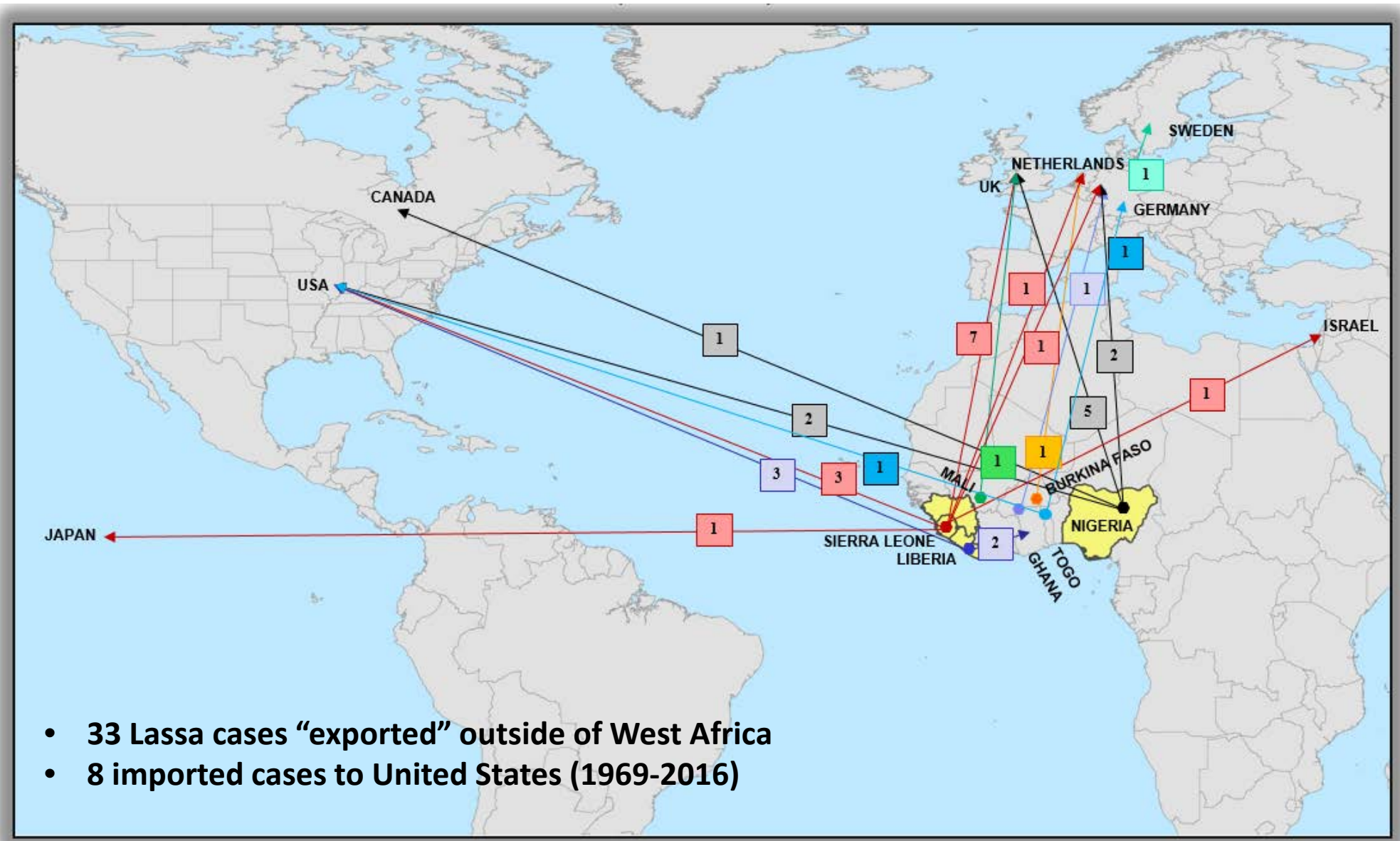


LASSA FEVER DISTRIBUTION MAP



¹McCormick et al. 1987

Global Impact



¹Macher et al. 2006

²Amorosa et al. 2010

³World Health Organization. 2015.

⁴Centers for Disease Control and Prevention. 2014.

⁵Raabe et al. 2017.

⁶Kitching et al. 2009

⁷Atkin et al. 2009

⁸World Health Organization. 2016.

⁹Grahn et al. 2016

Patient Characteristics	Total (n=33)
<u>Age (years)</u>	
Median	45
Range	18-72
<u>Sex</u>	
Male	22
Female	9
Not described	2
<u>Risk factors</u>	
Living or traveling in West Africa	18
Healthcare workers in West Africa	11
Travel to rural parts of West Africa or known rodent exposure(s)	4

Travel Characteristics	Total (n=33)
<u>Time of Year</u>	
Dry season (Nov-Apr)	20
Wet season (May-Oct)	10
Not described	3
<u>Nature of Travel from West Africa</u>	
Commercial airliner	20
Symptomatic at time of travel	12
Medically evacuated	10
Had known or suspect exposure to LF	6
Not described	3
<u>Presentation to care in destination country</u>	
Provider was aware of travel history	26
Provider unaware of travel history	4
Not described	3

Isolation Procedures	Total (n=33)
<u>Isolation</u>	
Isolated during hospital stay	24
Not isolated during hospital stay	8
Not described	1
<u>Nature and timing of isolation</u>	
Immediately isolated upon presentation	11
Contact +/- droplet +/- airborne precautions	8
Biocontainment unit	3
Isolated later in hospital stay	13
Contact +/- droplet +/- airborne precautions	2
Transferred to specialized hospital with specialized infection control capacity	11
<u>Time to isolation from hospital admission</u>	3-15 days

Contact Tracing	Total	Median	Range
Number of cases for whom contact tracing was performed	17	-	-
Number of all contacts traced	3420	157	3-552
Number of high-risk contacts traced	139	7	0-33

Secondary Transmission – Two Cases

- **First Case (2000)**

- Physician performing physical exam, obtaining IV access and blood samples without wearing personal protective equipment
- Completed oral ribavirin prophylaxis
- Remained asymptomatic
- Serologically converted (IgG 1:320 to same strain of Lassa Virus as patient)

- **Second Case (2016)**

- Mortician handling body of deceased patient; wore only gloves, no facial protection or apron
- Became ill with fever, sore throat
- Treated with IV ribavirin and oral favipiravir with resolution of illness

Challenge: Delay in suspicion of Lassa Fever

- Median of 5 days from presentation to clinical suspicion of Lassa
- Factors contributing to delay:
 1. Requires consideration of travel-associated illness not commonly seen outside of West Africa
 2. Travel to West Africa not always known at time of clinical presentation
 3. Even fever and distinctive clinical features only present in 59% of patients

Recommended PPE and Patient Placement for Patients with suspected Lassa* (stable or “dry” patients)

While evaluating and managing PUIs who are clinically stable and do not have bleeding, vomiting, or diarrhea, healthcare providers should at a minimum wear:

- Fluid-resistant gown that extends to at least mid-calf or single-use (disposable) fluid-resistant coveralls without integrated hood
- Full face shield
- Facemask
- Gloves with extended cuffs. Two pairs of gloves should be worn. At a minimum, outer gloves should have extended cuffs.

Patient Placement:

- Single patient room with closed door
- AIIR for AGPs

*Same guidance for Ebola, Marburg, Crimean-Congo Hemorrhagic Fever, and South American Hemorrhagic Fevers

Recommended PPE for unstable/"wet" patients with suspected Lassa* or confirmed patients with Lassa

While evaluating and managing PUIs who are clinically unstable and/or have bleeding, vomiting, or diarrhea, healthcare providers should at a minimum wear:

- Impermeable gown or coverall
- PAPR or N95 respirator + faceshield
- Examination gloves with extended gloves. Two pairs of gloves should be worn. At a minimum, outer gloves should have extended cuffs.
- Boot covers (or shoe covers in combination with coverall with integrated socks)
- Apron (optional)

Patient Placement:

- Single patient room with closed door
- AIIR for AGPs

*Same guidance for Ebola, Marburg, Crimean-Congo Hemorrhagic Fever, and South American Hemorrhagic Fevers

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Summary: IPC for Emerging Infectious Diseases

1. Early diagnosis key to instituting appropriate IPC measures
 - Challenges: Atypical clinical presentations and rarely-encountered nature of some of these illnesses
2. Appropriate IPC measures can protect HCP from nosocomial infections
 - Challenges: Nature of transmission, which informs IPC measures, may be incompletely understood; facility capability
3. Defining risk of exposures is critical to determining need for PEP and HCP monitoring and work restrictions
 - Challenge: HCP may not always notify occupational health about an exposure

Thank you!

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