MPOX DIAGNOSIS AND TREATMENT

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DISCLOSURES

- Grant/Research Support:
  - Previously: Study of Tecovirimat for Human Monkeypox Virus (STOMP)

- Employment:
  - Currently employed by BioNTech.

EXPLICIT IMAGES

- All images obtained and presented with patient consent

A CASE

- 28yoM presents for care complaining of painful genital lesions.
- History of uncontrolled HIV
- MPOX is diagnosed by PCR swab of lesions.
- Tecovirimat (TPOXX) is acquired via expanded access program through CDC and administered to the patient

A CASE

- Genital lesions worsened and patient developed disseminated lesions across body
- Vaccinia IV Ig was obtained from the CDC and administered
- Brincidofovir was obtained from the CDC and administered
- ART was initiated
- Lesions continued to progress and worsen

A CASE

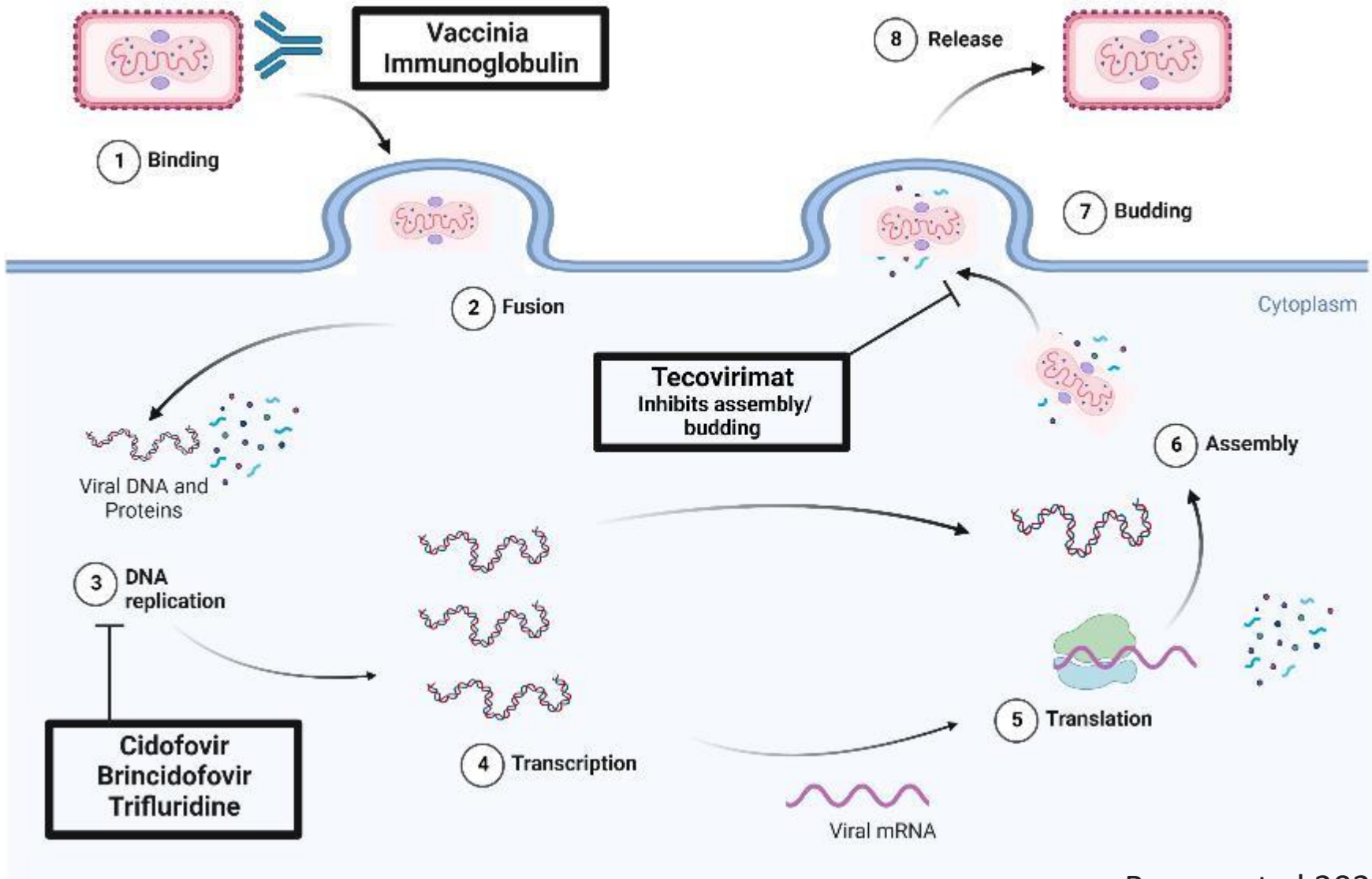
1 PATHOGENESIS

2 Clinical Manifestations and Diagnosis

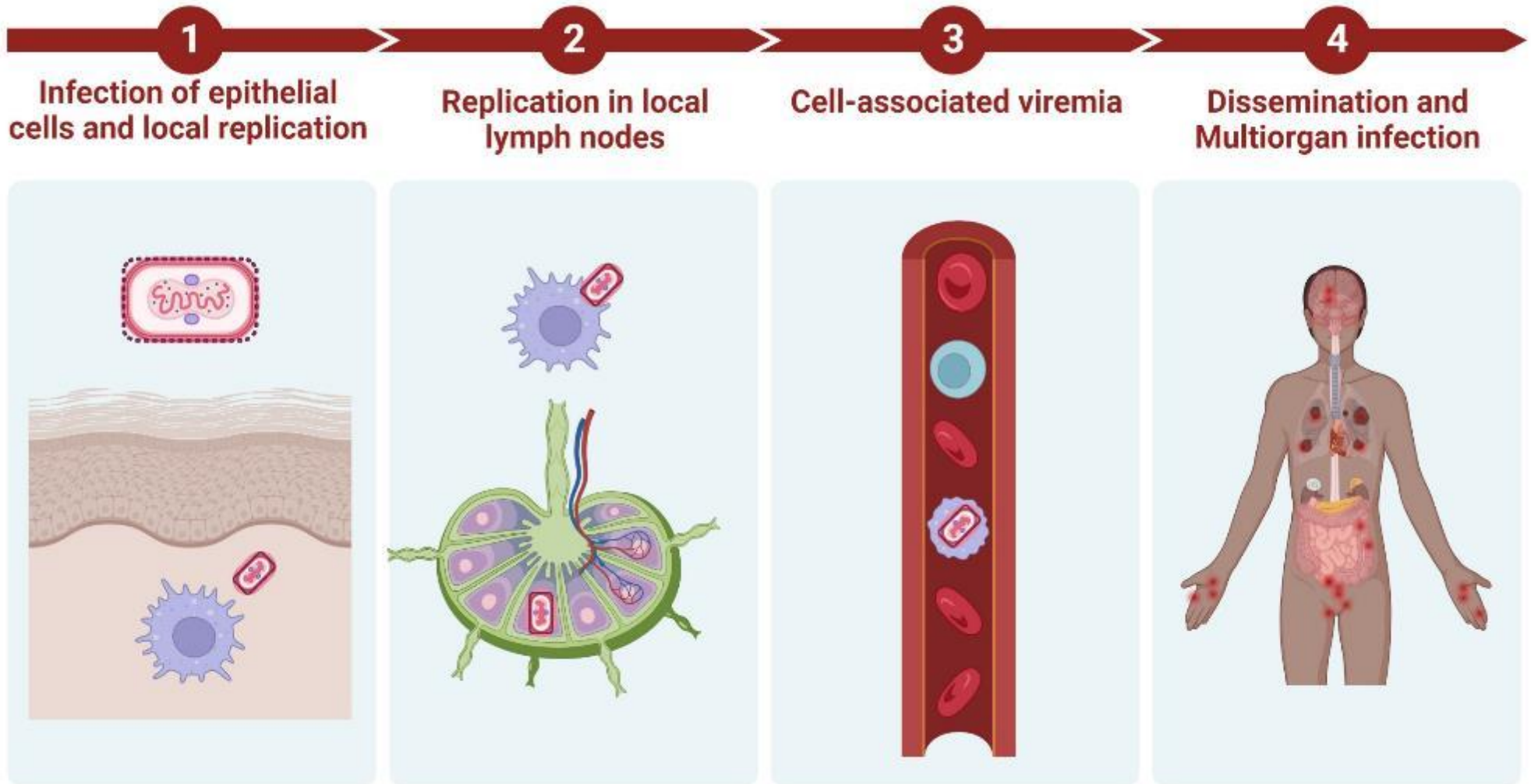
3 Overview of Treatment Options

4 Severe Cases: Lessons Learned

PATHOGENESIS



Barnes et al 2022



Shishido et al 2023

Incubation Period
7 Days (up to 21)

No symptoms

Transmission due to close contact often during sex
Possible: respiratory droplets
Possible: fomites from contaminated objects

Fever Curve

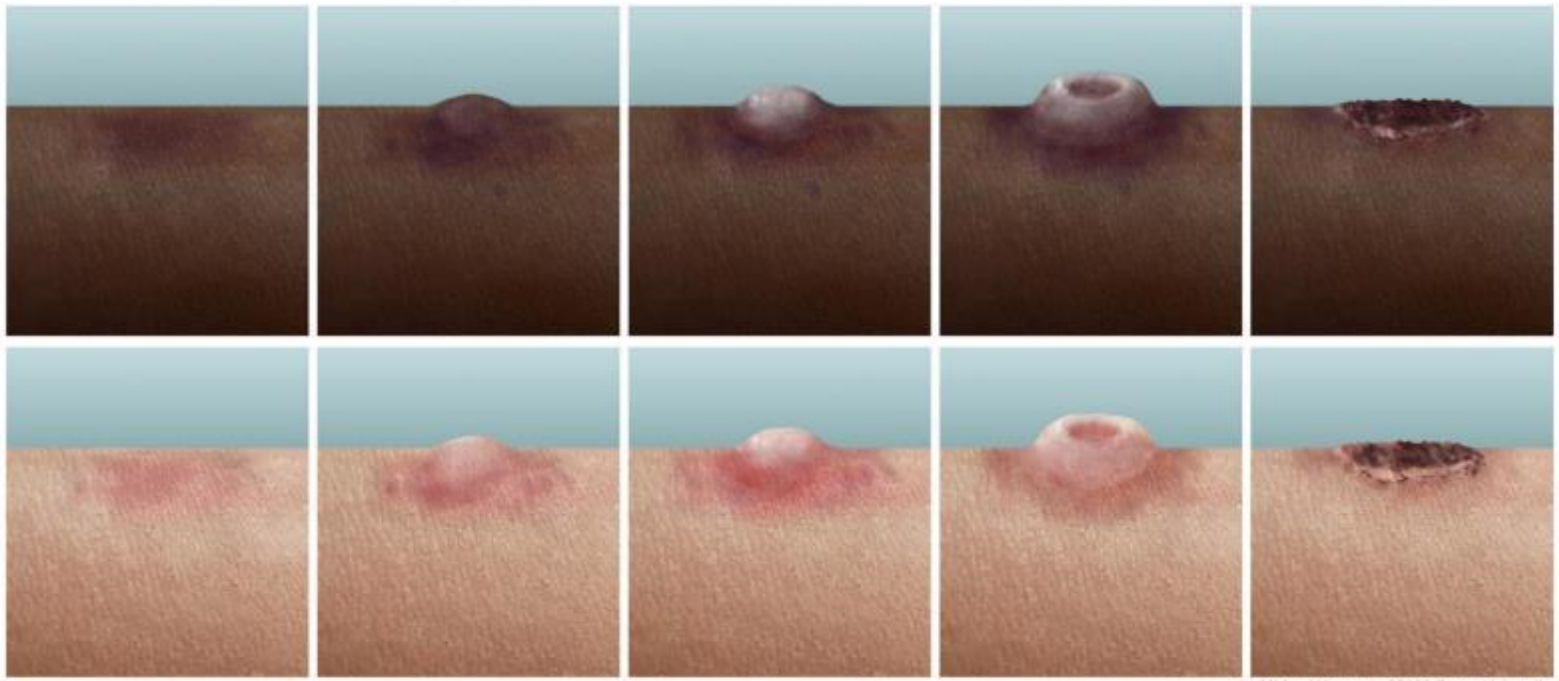
Prodrome
(absent in 40% cases)
Fever, headache, malaise

Single Lesion Develops often at site of inocculation

Dissemination
Lesions develop at multiple body sites.

Complications include: Proctitis, Urethritis, Conjunctivitis, encephalitis

Macules | Papules | Vesicles | Pustules | Scabs

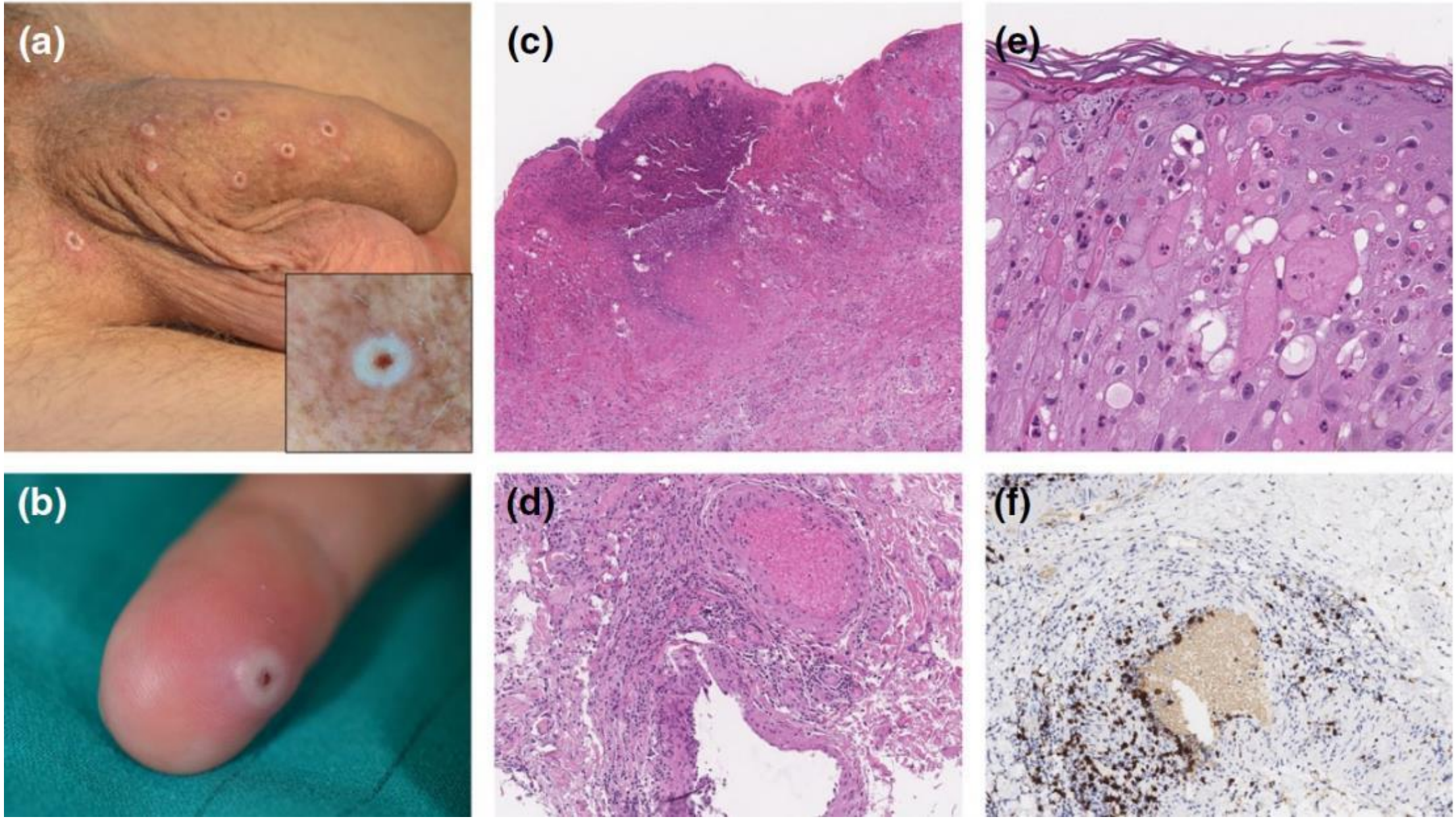


Michael Konomos ©2022 Emory University

Recovery
Lesions scab over and fall off

Once scabs fall off and reveal healthy underling skin, patient is no longer infectious

Weeks 1 2 3 4 5



Maronese CA et al, 2022

CLINICAL MANIFESTATIONS AND DIAGNOSIS

WHERE ARE PATIENTS PRESENTING?

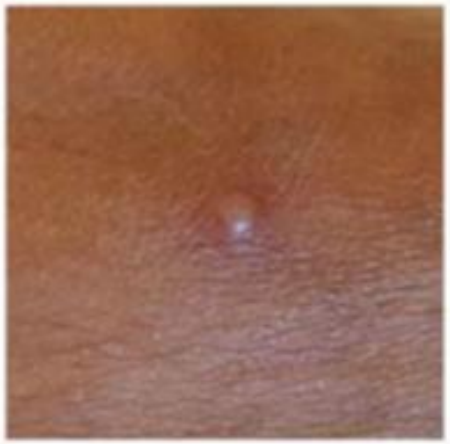
Table 3. Diagnosis and Clinical Characteristics of Monkeypox in the Case Series.*

Characteristic	All Persons (N=528)
Medical setting of presentation — no. (%)	
Sexual health clinic	120 (23)
Emergency department	106 (20)
Primary care	20 (4)
Dermatology clinic	38 (7)
HIV clinic	154 (29)
Other hospital clinic	30 (6)
Private clinics or other	60 (11)

CLINICAL FEATURES

- Rash may be located on hands, feet, chest, face, or mouth or near genitals
  - May look like pimples or blisters initially
  - Lesions can be painful or itchy
- May also have fever, chills, fatigue, muscle aches, respiratory symptoms (sore throat, cough, nasal congestion)
- Illness generally self-limited and lasts 2-4 weeks
- Differential diagnoses may include: secondary syphilis, chancroid, herpes, chickenpox/shingles

LESIONS CAN BE SUBTLE

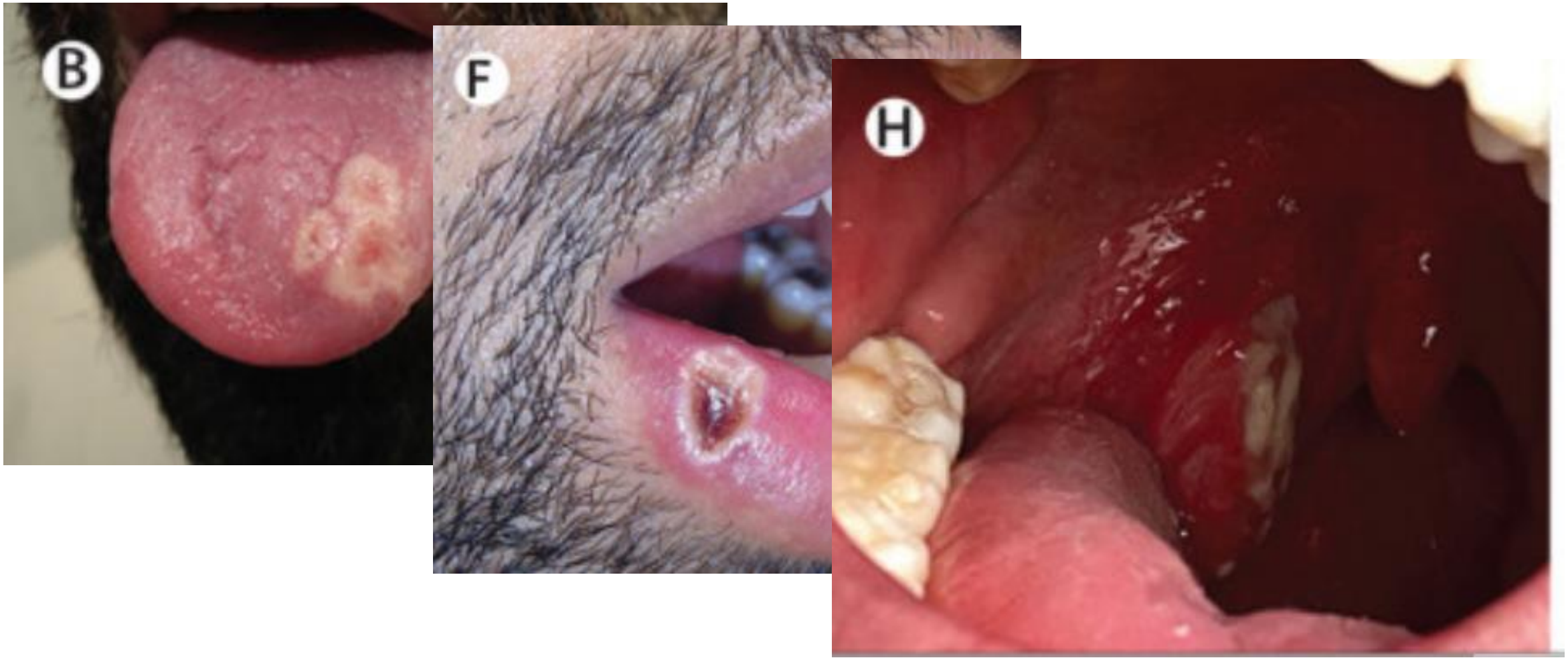




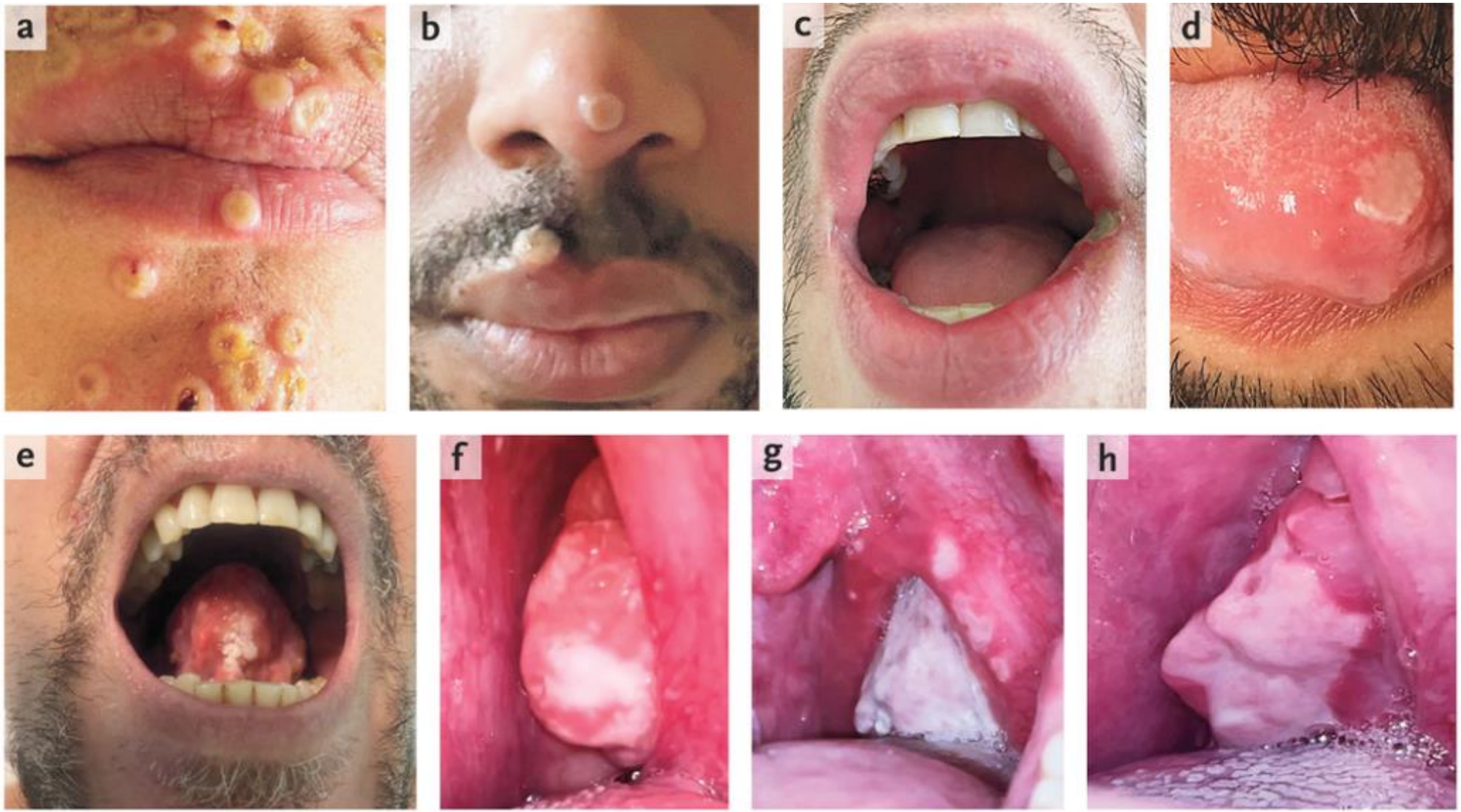


Mailhe et al 2022

ORAL LESIONS



Tarín-Vicente et al 2022



Thornhill et all 2022

CASE DEFINITIONS FOR MPOX

- **Confirmed:** Meets confirmatory laboratory criteria *(Monkeypox virus detected)*
- **Probable:** Meets presumptive laboratory criteria *(Orthopoxvirus or IgM antibody detected)*
- **Suspected:** Meets either new characteristic rash or clinical suspicion with at least 1 of these epi criteria:
  - Close/sexual contact
  - Travel outside US
  - Animal or animal product

TESTING: RT-PCR

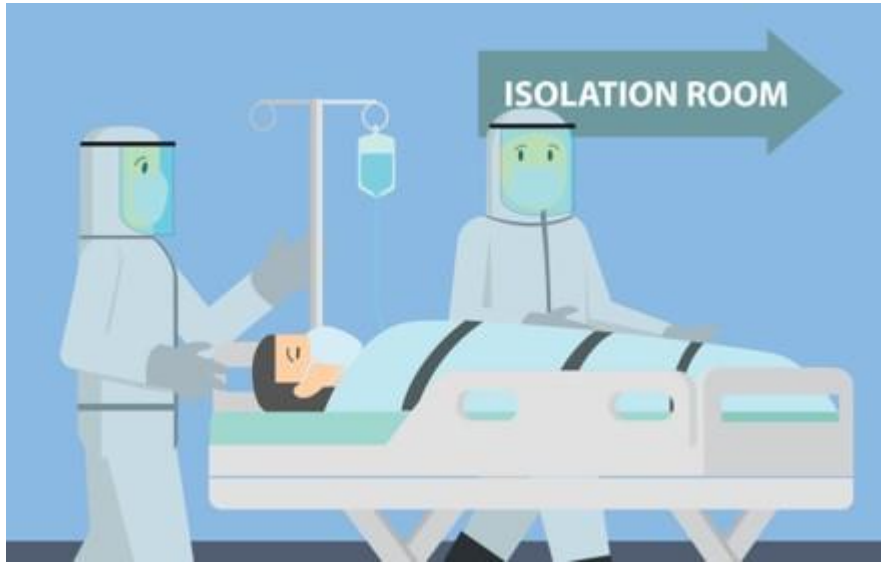
- Virginia's State Lab (DCLS)
- RCHD Contact Line: 804-205-3501

- Commercial Labs: Mayo, Labcorp, Quest Diagnostics, Aegis Sciences and Sonic Healthcare – no 'approval' required
- Wear PPE!
- VIGOROUSLY swab lesions
- (DO NOT UNROOF)
- Submit swabs from multiple lesions
- Refrigerate or place on ice

- Notify VDH of + patients

CDC Guidelines for Collecting Specimens for Mpox Testing
Monkeypox Virus Infection Resulting from an Occupational Needlestick — Florida, 2022

INFECTION PREVENTION AND CONTROL



- Isolate patient in single room
  - Use PPE: gown, gloves, N95 respirator, eye protection
  - Limit patient transport
- Avoid activities that may spread material from lesions
- Contact LHD immediately to report case

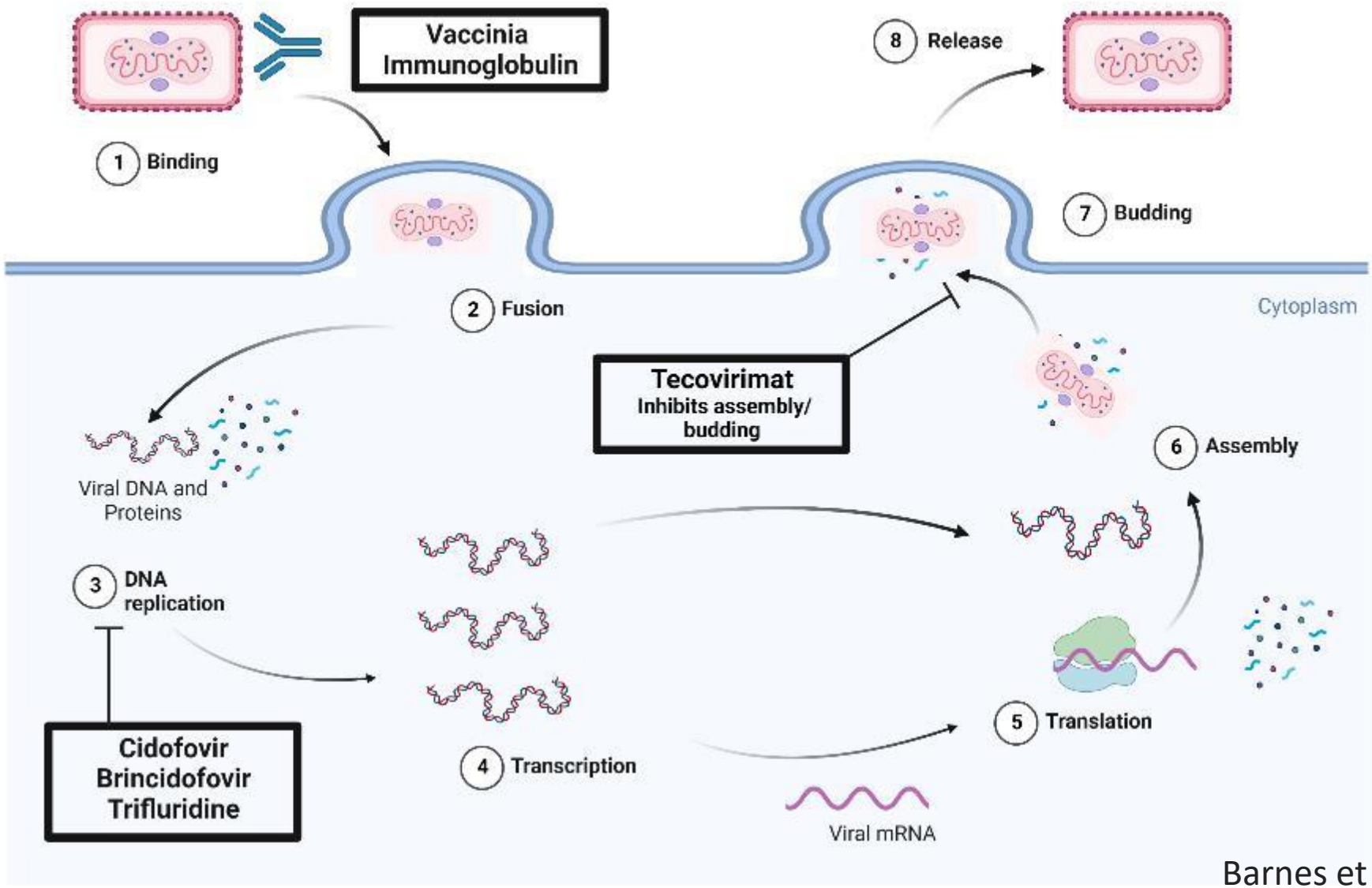
  LHD Locator: vdh.virginia.gov/health-department-locator/

OVERVIEW OF TREATMENT OPTIONS

SUPPORTIVE CARE FOR ALL PATIENTS

- Assess and provide supportive care for pain management, skin and oral lesions, proctitis, gastrointestinal symptoms

- Examples include:
  - Over-the-counter or prescription pain medications
  - Rehydration for fluid losses
  - Anti-emetics for nausea and vomiting
  - Sitz baths for proctitis or painful lesions
  - Wound Care, follow up



Barnes et al 2022

VACCINIA IMMUNOGLOBULIN

- FDA approved for complications of smallpox vaccination
  - Eczema vaccinatum, PV, generalized vaccinia, ocular vaccinia
- Available through SNS*
- No Monkeypox Data
- Recommendation for use in smallpox extrapolated from vaccinia data (also poor – uncontrolled case series, case reports)

CIDOFOVIR, BRINCIDOFOVIR

- Cidofovir – (CMV) Inhibits viral DNA polymerase
  - In vitro and In Vivo data against poxviruses including monkeypox (1)
  - Case reports of use in vaccinia (1)
  - Readily available
    - High renal toxicity
    - No PO options (IV or TOPICAL)

- Brincidofovir - oral prodrug of cidofovir
  - Must request from CDC
  - Limited data – in one case series – all patients had to discontinue due to hepatitis (2)

TRIFLURIDINE

- licensed for the treatment of herpes keratoconjunctivitis/keratitis
- In vitro evidence of activity against orthopoxviruses
- Case reports of use for ocular orthopoxvirus infections (vaccinia)

TREATMENT OPTIONS: TPOXX

- **CDC offers clinical consultation service (email eocevent482@cdc.gov) or call CDC Emergency Operations Center at 770-488-7100**
- Tecovirimat may be considered for people
  - With **severe disease** (e.g., hemorrhagic disease, confluent lesions, sepsis, encephalitis, ocular or periorbital infection, or other conditions requiring hospitalization)
  - With involvement of **anatomic areas** that might result in serious sequelae that include scarring or strictures
  - Who are at **high risk of severe disease**:
    - People with severe immunocompromise
    - Pediatric patients, particularly those younger than 1 year of age
    - Pregnant or breastfeeding women
    - People with a condition affecting skin integrity

CDC Treatment Information for Healthcare Professionals

CONSIDERATIONS WITH TPOXX

- Clinicians and patients should understand
  - Limited tecovirimat effectiveness data in people with mpox
  - Lack of data indicating which patients might benefit the most
  - Concern for development of resistance that could render the drug ineffective for any treated patients

- Oral or IV, 14 day course – but can be expanded depending on clinical scenario

CDC Guidance for Tecovirimat Use

TPOXX RESISTANCE

- CDC Health Update on November 17, 2022, reported two cases of lab-confirmed TPOXX resistance.
  - Both patients were severely immunocompromised, with progressive infection despite prolonged TPOXX treatment (>14 days)
  - Viral resistance is rare
  - Encourage testing for TPOXX resistance and pharmacokinetics in patients who have persistent or progressive mpox after 14 days of TPOXX
  - Counsel patients about critical importance of taking oral TPOXX with fatty meals to ensure adequate gastrointestinal absorptions and maximize serum levels of the drug

- Recent article reported TPOXX resistance was infrequent and occurred in immunocompromised patients (uncontrolled HIV infection with very low CD4+ T-cell counts and potential for extensive tecovirimat exposure while hospitalized)

CDC Guidance for Tecovirimat Use

STUDY OF TECOVIRIMAT ON HUMAN MPOX VIRUS (STOMP) CLINICAL TRIAL

Call Center: 1-855-876-9997 (U.S. only)

STOMP About the Study Participating Research Sites FAQs

NOW ENROLLING REMOTELY ACROSS THE UNITED STATES!

Call today for more information: 1-855-876-9997

[Study of Tecovirimat for Human Monkeypox Virus]

TREATMENT OPTIONS

Treatment Option	Indication	Formulations Available
Tecovirimat (TPOXX or ST-246) *Antiviral	Per EA-IND, for patients with laboratory confirmed non-variola orthopoxvirus infection or suspected infection based on known exposure(s) and/or clinical manifestations of disease	Oral (200 mg capsule)* Injection for intravenous administration *ability to mix with semi-solid food for pediatrics < 13 kg
Cidofovir (Vistide) *antiviral	FDA approved for treatment of cytomegalovirus retinitis in patients with AIDS	Intravenous infusion single-unit vial once weekly
Vaccinia Immune Globulin Intravenous (VIGIV)	FDA licensed for treatment of complications due to vaccinia vaccination	Intravenous infusion single-dose vial
Brincidofovir (Tembexa) *antiviral	FDA approved for the treatment of smallpox in adults and pediatrics, including neonates *As of 10/31/22, available from SNS through an e-IND request to FDA.	Oral (100 mg tablet or 10 mg/mL suspension) once weekly for 2 doses

SEVERE CASES: LESSONS LEARNED

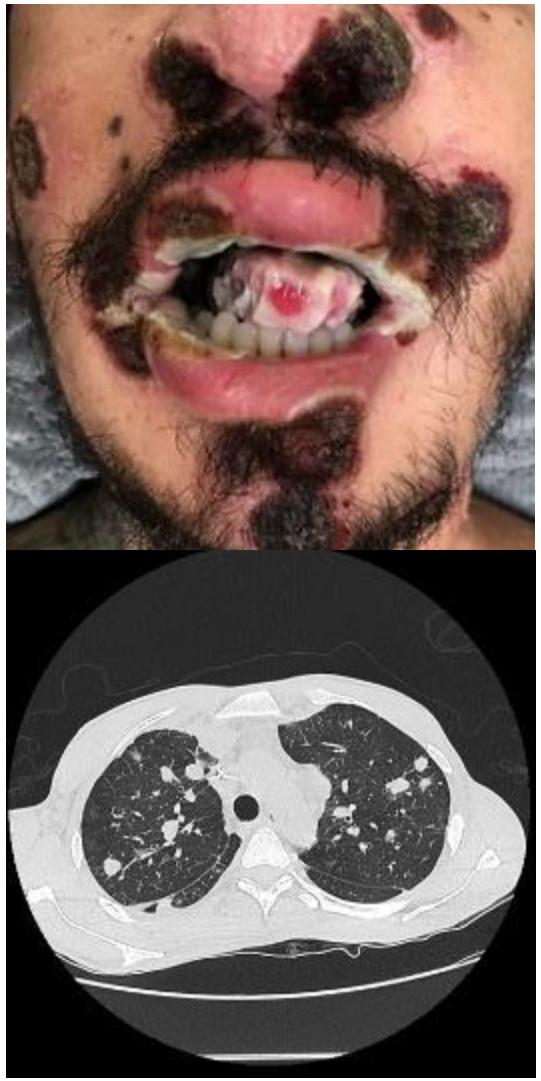
BACK TO OUR CASE

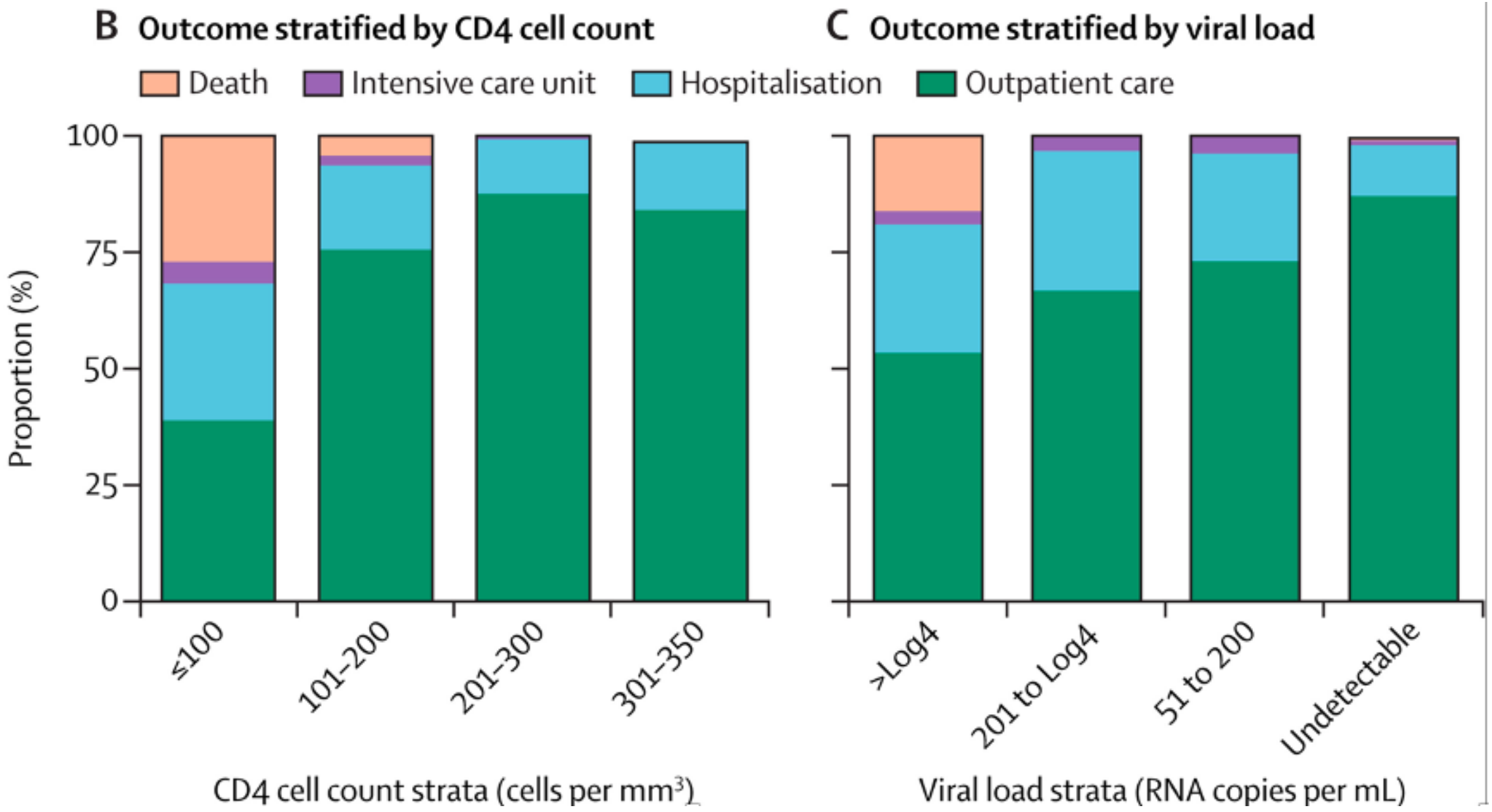
- Genital lesions worsened and patient developed disseminated lesions across body
- Continued on TPOXX
- Vaccinia IV Ig was obtained from the CDC and administered
- Brincidofovir was obtained from the CDC and administered
- ART was initiated
- Lesions continued to progress and worsen
- Patient developed multiorgan failure and died on day 68 from diagnosis, 3 weeks after starting ART

Carrubba et al. 2023

IMMUNOCOMPROMISED HOSTS

- **HIV**
  - **Well controlled HIV – like non-HIV infected patients**
  - **Uncontrolled HIV:**
    - more prolonged illness, larger lesions, and higher rates of both secondary bacterial skin infections and genital ulcers, strictures/scarring, bowel obstruction/perforations, lung involvement, necrosis, encephalitis, myocarditis, sepsis and death (1-4)



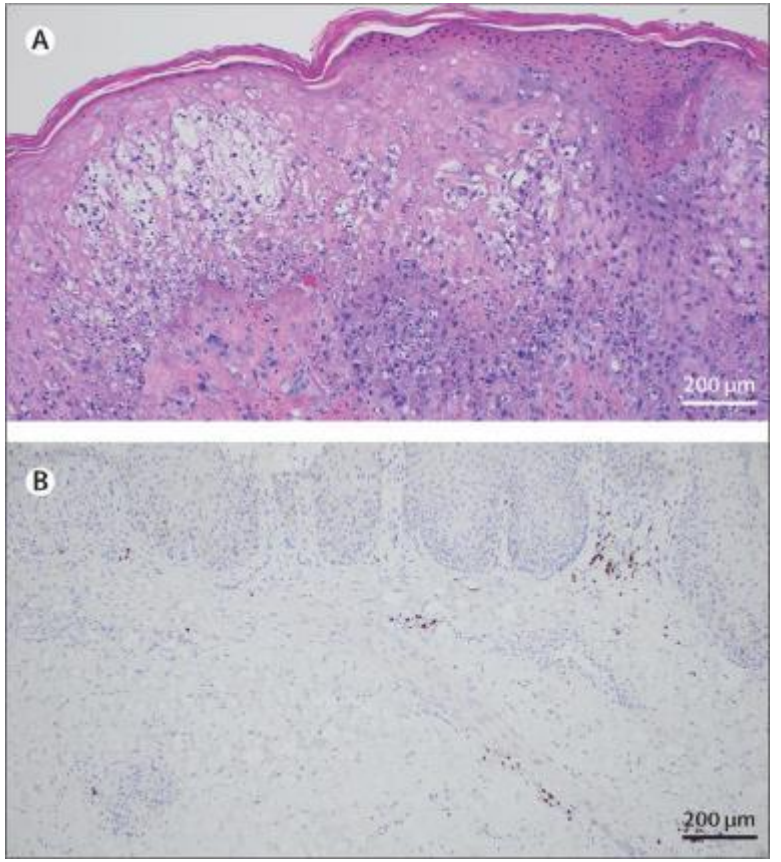

B Outcome stratified by CD4 cell count
C Outcome stratified by viral load
Death
Intensive care unit
Hospitalisation
Outpatient care
Proportion (%)
100
75
50
25
0
≤100
101–200
201–300
301–350
>Log4
201 to Log4
51 to 200
Undetectable
CD4 cell count strata (cells per mm³)
Viral load strata (RNA copies per mL)

SEVERE MPOX IN IMMUNOCOMPROMISED PATIENTS WITH HIV OR OTHER CONDITIONS

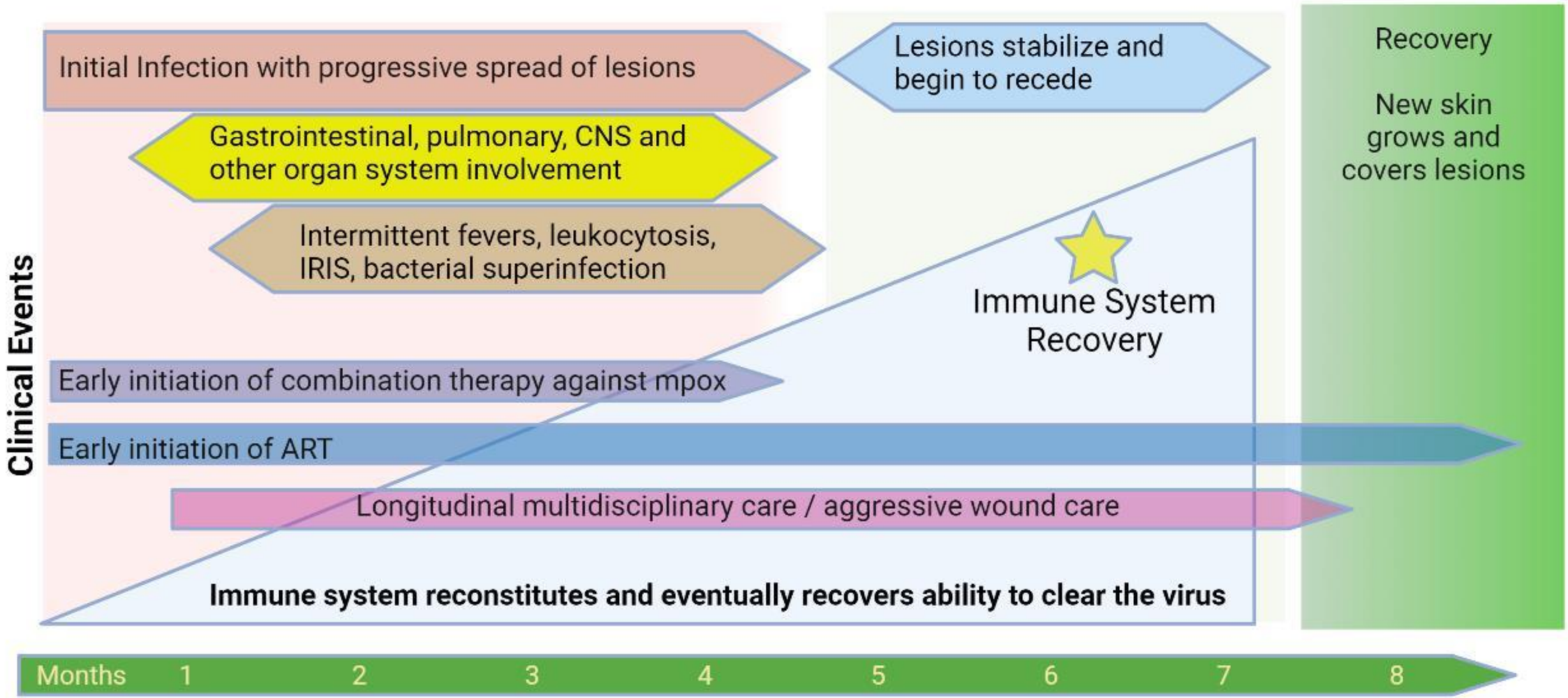
- CD4 T cells are required to clear the virus
- No recovery can begin until the immune system has reconstituted
- IRIS?

- Resistance against TPOXX, while rare is possible
- In vitro and In vivo evidence of synergy with combination TPOXX and brincidofovir.

- **Therefore, recommend immediate initiation of combination antiviral therapy against mpox (TPXOX+VIGIV+CIDOFOVIR) AND ART at earliest possible time**



Shishido et al, Carrubba et al. 2023



Shishido et al 2023

MPOX AND HIV (CONTINUED)

- For people with HIV diagnosed coincident with mpox or who are not taking ART, CDC recommends starting ART as soon as possible, and in consultation with an expert in HIV medicine if needed

- STI screening for sexually active persons evaluated for mpox, treat if test positive

- Virologic and Immunologic Characteristics of Severe Mpox in People with Advanced HIV (VIRISMAP) Study to determine why some patients have severe mpox and understand pathogenesis

Clinical Considerations for Treatment and Prophylaxis of Mpox Infection in People Who are Immunocompromised

SEVERE MPOX IN IMMUNOCOMPROMISED PATIENTS WITH HIV OR OTHER CONDITIONS

- Consult CDC Monkeypox Response Clinical Escalations Team at eocevent482@cdc.gov or 770-448-7100

CDC Severe Manifestations of Monkeypox among People who are Immunocompromised Due to HIV or Other Conditions

CDC Severe Monkeypox in Hospitalized Patients — United States, August 10–October 10, 2022

Day 29 Day 53 Day 239

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THANK YOU!