Infectious Disease in the News

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South Texas HFMA Annual Symposium

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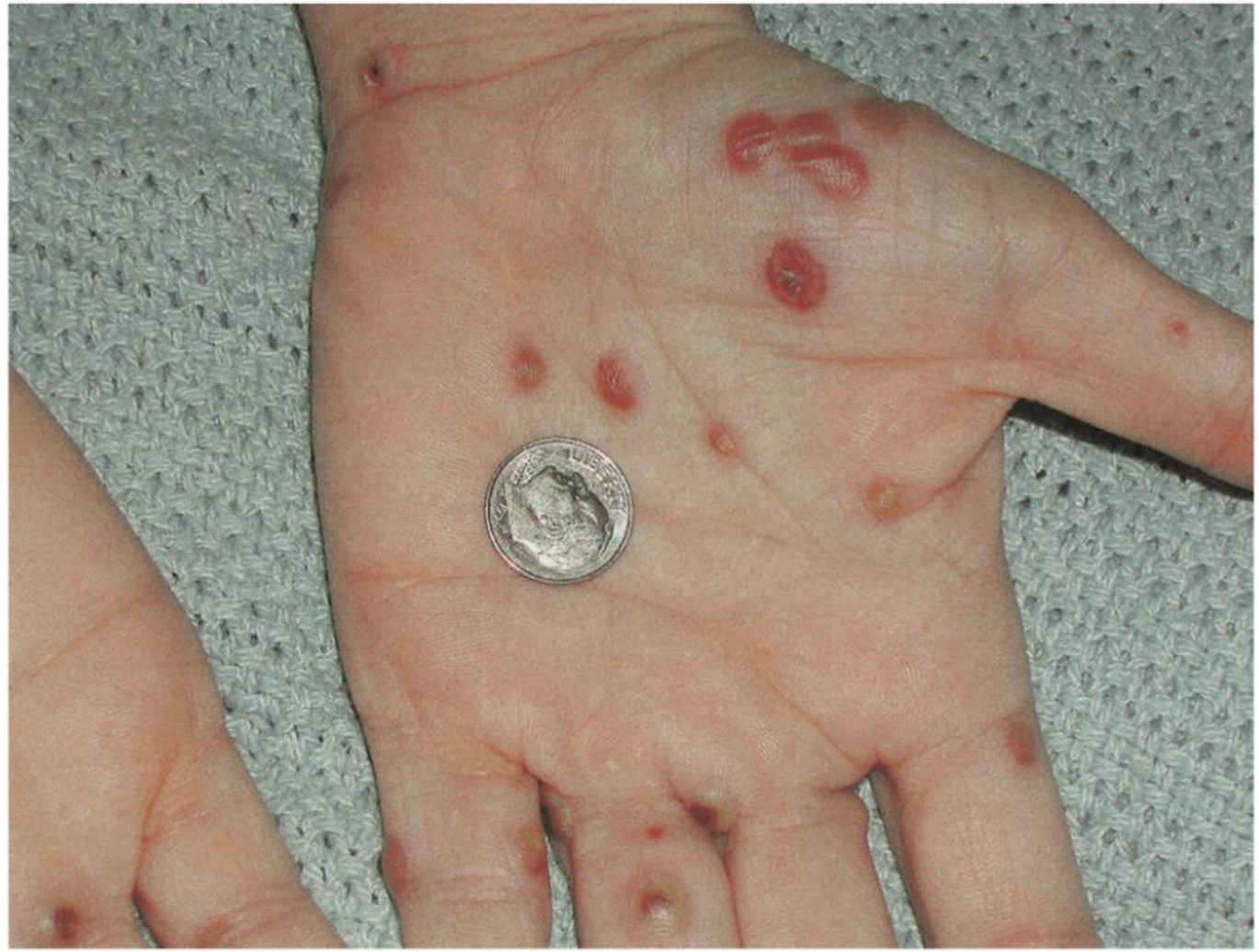
UT Health San Antonio

Conflicts of Interest

- None

Case

- 26 yo male presents to your primary care clinic with a 5 day history of headache, fever, swelling in the groin, and 3 days of rash
- He has no PMHx, currently on PrEP with daily emtricitabine and tenofovir disoproxil fumarate (Truvada), no recent travel history
- He identifies as gay, reports recent history of unprotected oral and anal sex with multiple male partners via dating apps
- Exam: febrile, cervical and inguinal LAD, vesicular rash on trunk, extremities, groin all in the same stages of development



What is the most likely causative agent?

A. Syphilis

B. Smallpox

C. Varicella

D. Monkeypox

Objectives

1. Discuss the history, epidemiology, pathophysiology of monkeypox
2. Discuss the clinical signs/symptoms, presentation of monkeypox
3. Discuss the differential diagnosis of acute vesicular lesions
4. Discuss the current state of monkeypox outbreak
5. Explore potential treatment options and vaccine management
6. Outline steps that primary care providers can take to identify, report, treat monkeypox

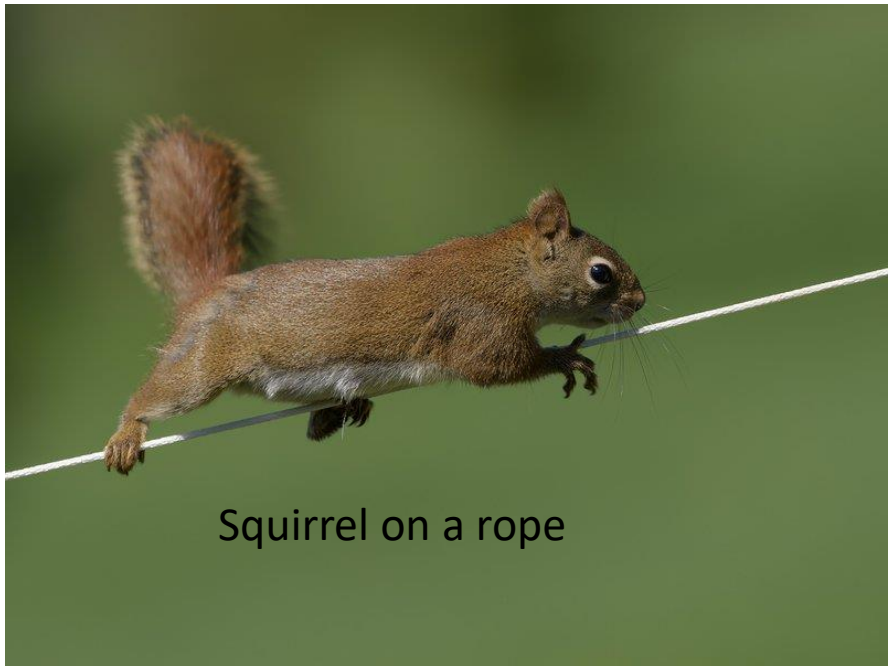
Monkeypox

- Viral zoonotic infection
- First detected in captive Asiatic monkeys in 1958 – shipped from Singapore to a Denmark research facility
- First human case 1970 – DRC, virus isolated from a child suspected to have smallpox
- Naturally only in Africa – rural areas
- In US/worldwide due to global commerce, travel
- Rodents – important reservoir hosts, squirrels, giant pouched rats

Map of Africa showing countries reporting human Monkeypox cases (1971–2019).

Infect Dis Clin North Am. 2019 Dec;33(4):1027-1043. doi: 10.1016/j.idc.2019.03.001.

Rope squirrel

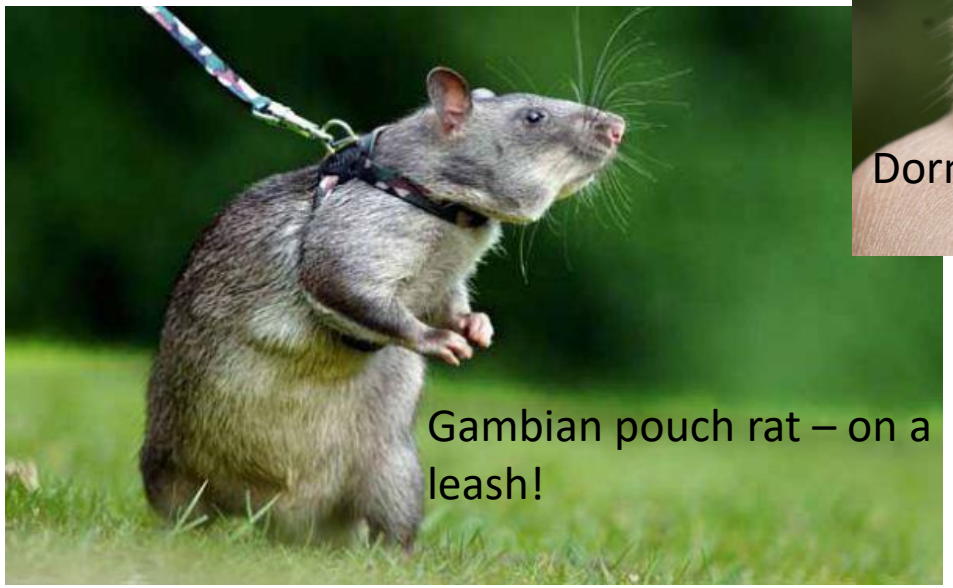


Squirrel on a rope

Elephant shrew – spewing droplets

Dormouse

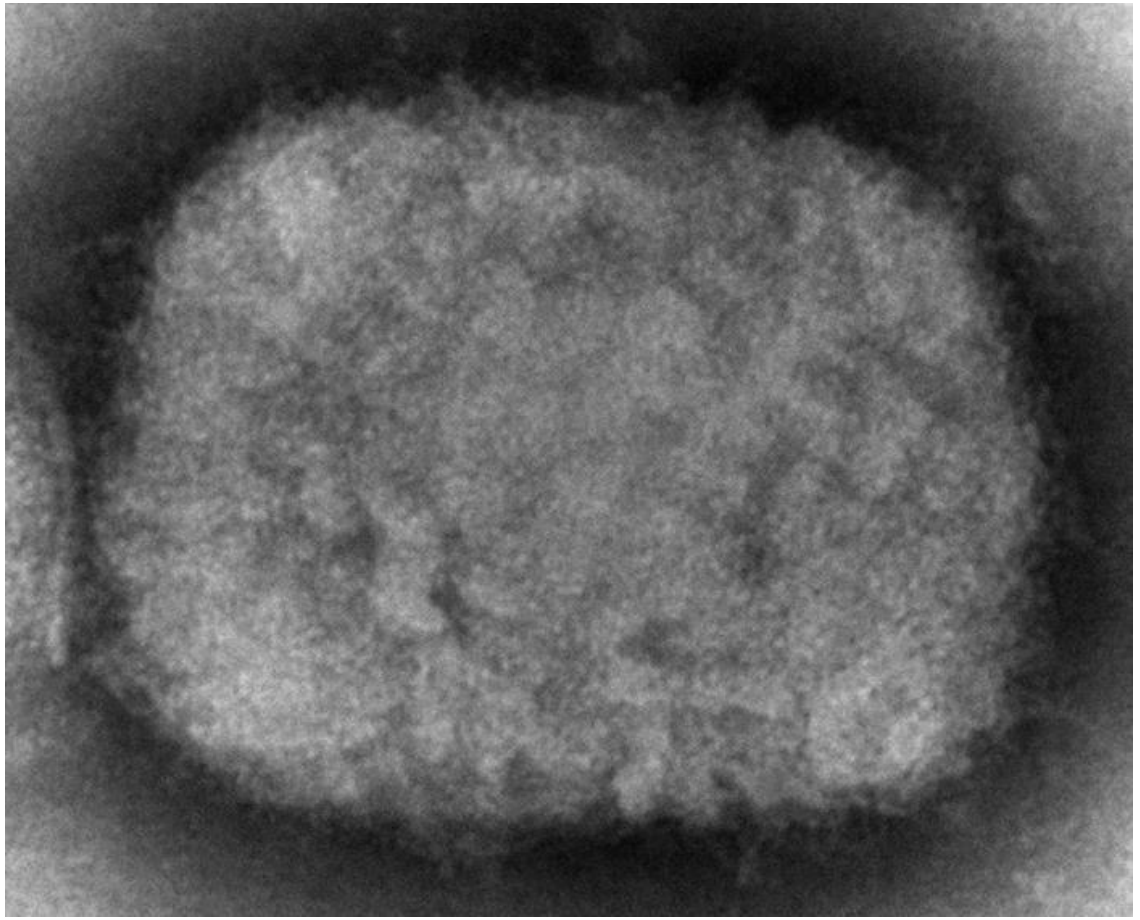
Gambian pouch rat – can detect TB



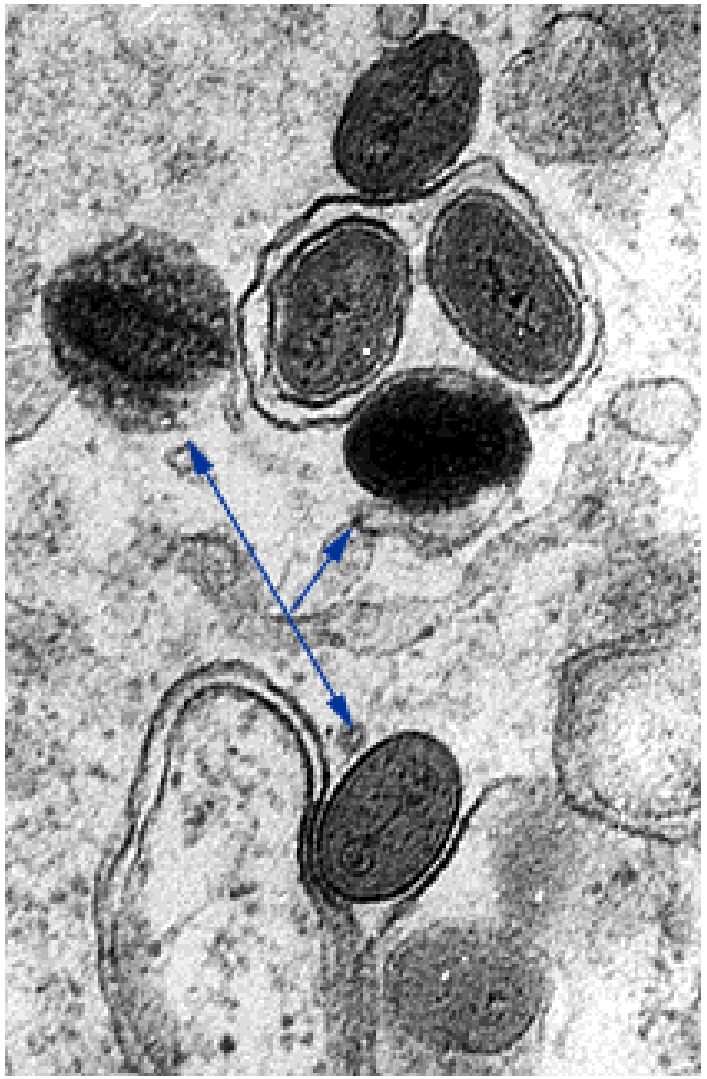
Gambian pouch rat – on a leash!

Zoonotic orthopox virus

- One of the 4 orthopoxvirus species pathogenic for humans
  - Variola major – smallpox
  - Variola minor – strain of smallpox
  - Cowpox
  - Infections have been described from vaccinia virus (the virus used for the smallpox vaccine), cowpox, buffalopox, camelpox
- Large (200-250 nanometers), brick shaped, lipoprotein envelope with linear DS-DNA genome
- Reliance on host ribosomes for mRNA translation, otherwise includes all necessary replication, transcription, assembly, egress proteins in the genome
- Two genetically distinct strains
  - Western African clade (II, with IIa and **IIb**) – less virulent, lack a number of genes present in the Central African strain
  - The Congo Basin (Central African) clade (I) is reported more frequently than the West African clade and has documented cases of human-to-human transmission, higher case fatality rate



Poxvirus under electron microscopy. Public Health Image Library #22663



Intracellular brick-shaped vaccinia virions with dense central core and outer viral membranes (blue arrows)

Herrera E, del mar Lorenzo M, Blasco R, Isaacs SN. J Virol 1998; 72:294.

CDC Alerts

- November 2021 – travel associated case in Maryland, travel to Nigeria
- July 2021 – travel associated case in Texas, travel to Nigeria
- 2003 – 47 (53?) confirmed and probable cases from six states, Illinois, Indiana, Kansas, Missouri, Ohio, Wisconsin, all became ill after contact with pet prairie dog, first time monkeypox was reported outside of Africa
  - Contact with sick animal
  - Bite or scratch that broke the skin
  - Cleaning cage, touching bedding
  - None were attributed to person-to-person contact
- CDC, public health dept, USDA, FDA – extensive lab testing, smallpox vaccine and treatments, guidance for patients, healthcare providers, vets, animal handlers, tracking potentially infected animals, investigating human cases, immediate embargo and prohibition of importing, interstate transportation, sale, release into environment certain rodents

USA

- 2003 – human infections because of contact to ill prairie dogs
- Six states: Illinois, Indiana, Kansas, Missouri, Ohio, Wisconsin
- Exposure to West African small mammals imported as exotic pets
- Imported to US April 9, 2003 – shipment of small mammals
- Gambian rat, rope squirrel, dormouse from affected African shipment of exotic species originating from Ghana – stored next to prairie dogs
- Viral isolation and nucleic acid detection

https://www.nationalgeographic.com/animals/mammals/facts/prairie-dogs

International Cases

- September 2018 – 3 cases in UK, two with recent travel one healthcare worker caring for the patients
- October 2018 – man traveled from Nigeria to Israel
- May 2019 – man traveled from Nigeria to Singapore
- May 2021 – family returned to UK after travel to Nigeria, 3 family members sick, timing (day 0, 19, 33) suggested human to human transmission
- July 2021 – man traveled from Nigeria to Texas
- November 2021 – man traveled from Nigeria to Maryland

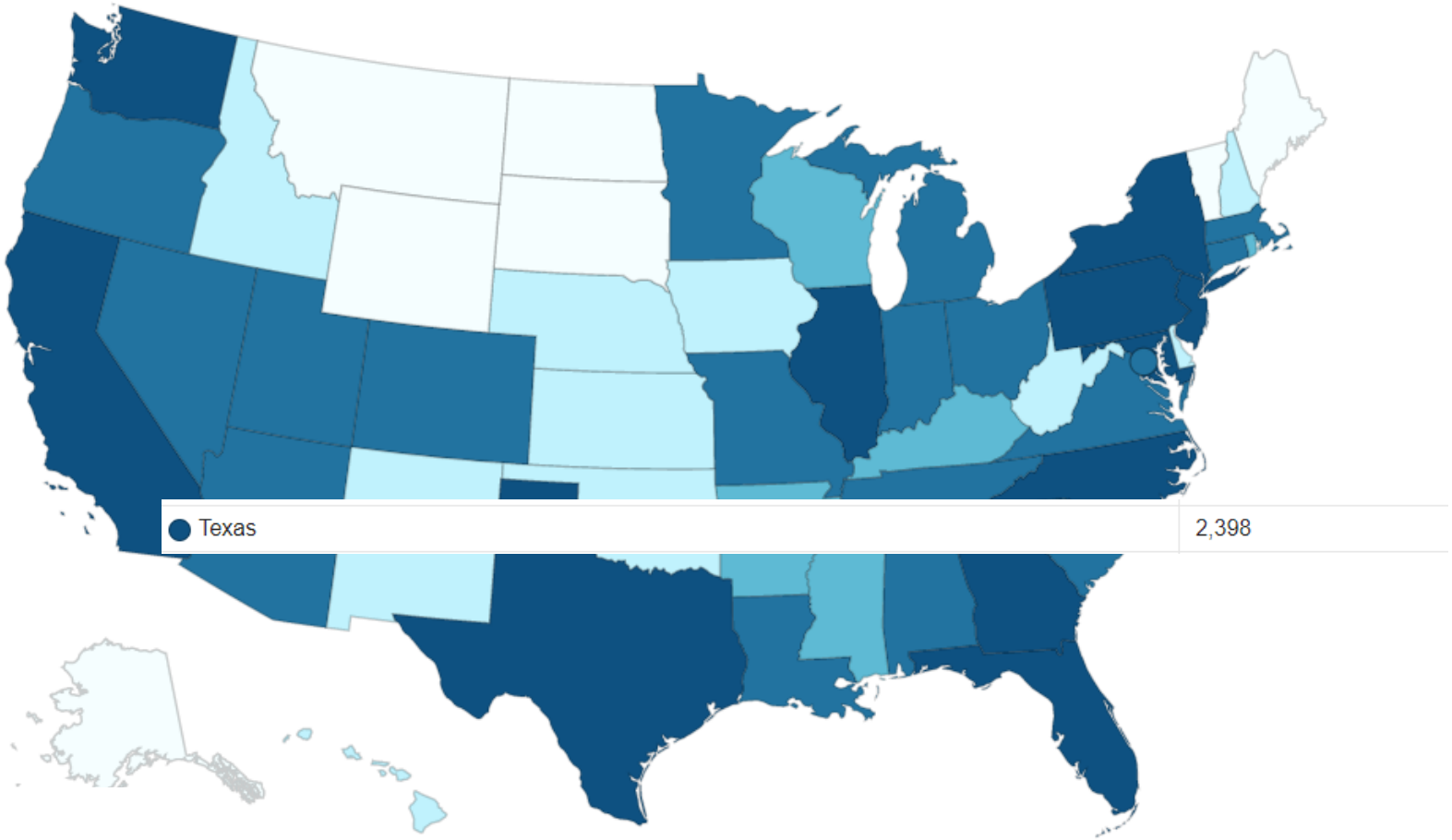
May 2022

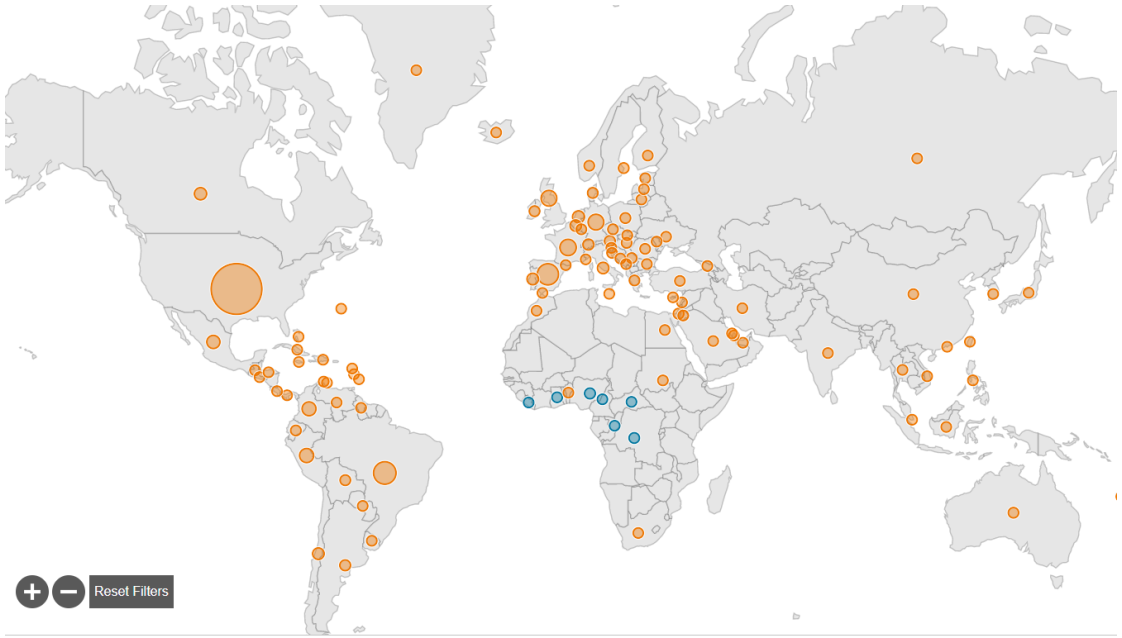
- May 13, 2022 WHO recognizes cases in countries that are not endemic, clusters of cases in Portugal, Spain, UK (May 7 case recent travel, one week later six additional cases, no travel or close contact)
- May 18, 2022 – Case reported in Massachusetts, travel to Canada
- WHO and CDC tracking cases
- No established travel links to endemic areas
- Mainly but not exclusively in MSM seeking care in primary care or sexual health clinics (detection bias?)
- Travel, specific risk factors, gender, sexual orientation
- Not known if direct connection between cases, may spread within certain communities due to close contact

As of October 5, 2022

26,311 Total confirmed monkeypox/orthopoxvirus cases

*One Florida case is listed here but included in the United Kingdom case counts because the individual was tested while in the UK.





Legend

- Has not historically reported monkeypox
- Has historically reported monkeypox

Confirmed Cases

70,420	69,702	718
Total Cases	in locations that have not historically reported monkeypox	in locations that have historically reported monkeypox

Locations with cases

107	100	7
Total	Has not historically reported monkeypox	Has historically reported monkeypox

Transmission

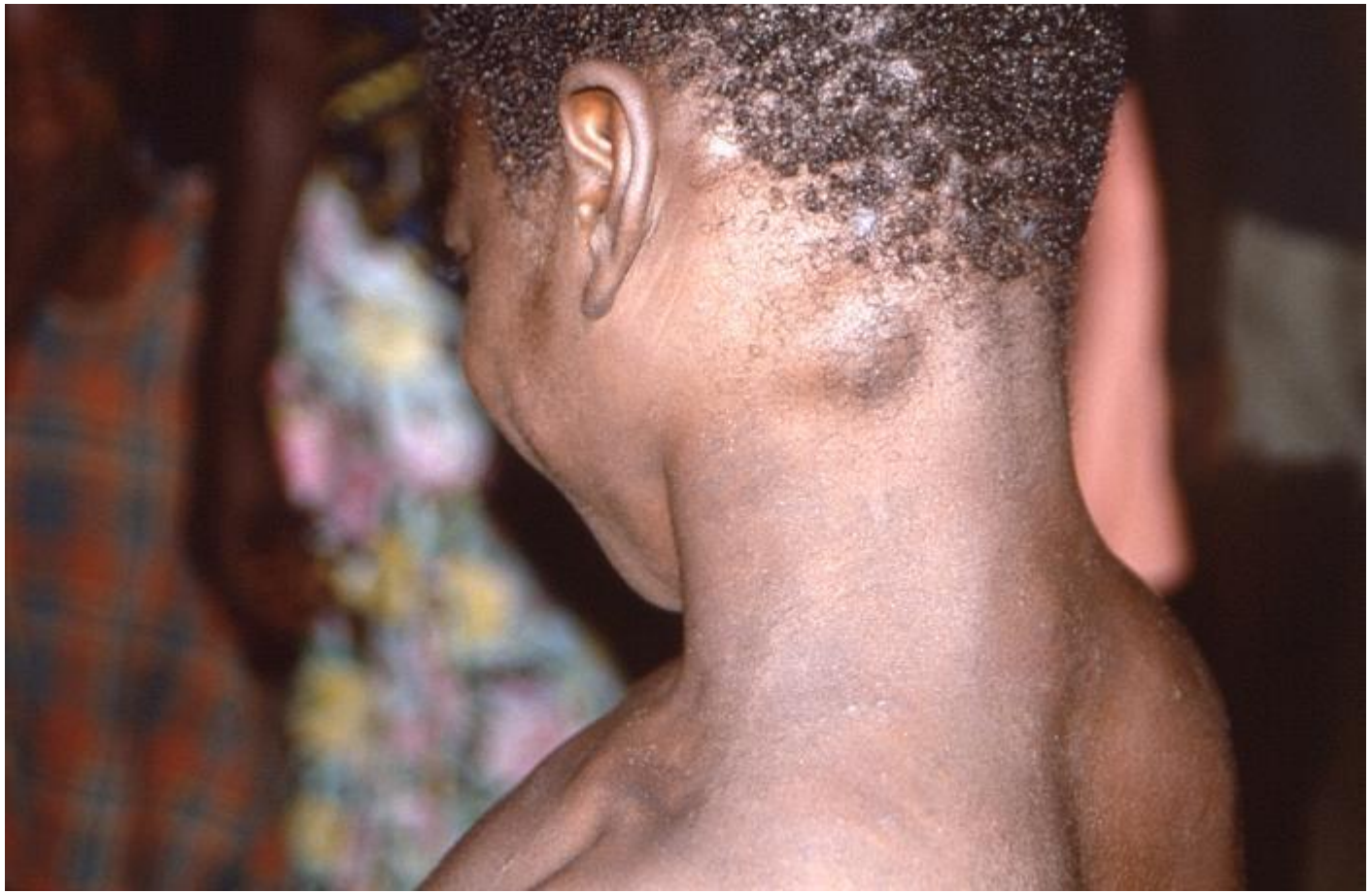
- Animal to human
- Human to human
- Fomites
- Crosses placenta
- Bite or scratch
- Handling wild game, use of products from infected animal
- Direct contact – body fluids, skin lesions, respiratory droplets
- Human to human – direct contact, respiratory secretions (prolonged face to face contact), sexual or intimate contact (decreasing herd immunity to orthopoxviruses) within 6 feet, more than three hours without PPE

Pathogenesis

- Viral entry from any route (nose, mouth, skin) replicates at inoculation site and spreads to local lymph nodes
- Viremia – seeds other organs
- Incubation period 7-14 days, upper limit 21 days (animal bite or scratch may have shorter incubation period)
- Prodromal symptoms -> acute febrile exanthem
- Greater degree of lymphadenopathy
- Lower capacity for human-to-human spread (vs smallpox)
- Source of infection
- Mode of transmission may correlate to severity

Clinical Manifestations

- Classic or modified case of smallpox
- Fever, headache, myalgias, fatigue
- Pronounced lymphadenopathy – submandibular, cervical, sublingual regions
- Mucosal lesions
- Rash within 1-3 days *after appearance* of fever, starting on face, oropharynx, spreading to other parts of body, includes the palm and soles
- Rash evolves over 2-4 weeks: 1-2 day increments
- Complications: bacterial skin infections, respiratory, GI, keratitis
- Mortality ~10%



Cervical lymphadenopathy in a child with monkeypox. Public Health Image Library #12778

Rash

- Begins on the face, trunk, spread to other areas, including palms and soles, site of inoculation (genital, groin regions)
- Stages – macules, papules, vesicles, pustules, umbilication, scabs, desquamation (some with only localized rash at site of direct contact)
- Change synchronously
- Firm, deep seated 2-10 mm in size
- Pustular phase 5-7 days before crusts form
- Crusts, desquamate 7-14 days
- Condition resolved 3-4 weeks after symptom onset in most cases
- No longer infectious after crusts fall off

US 2003 Outbreak – further characterization

- Rash (97 percent)
- Fever (85 percent)
- Chills (71 percent)
- Lymphadenopathy (71 percent)
- Headache (65 percent)
- Myalgias (56 percent)
- 9 of 34 patients required hospitalization, N/V, dysphagia
- Encephalopathy, retropharyngeal abscess
- Non-specific lab abnormalities: abnormal LFTs, leukocytosis, thrombocytopenia, hypoalbuminemia

Clin Infect Dis. 2005 Dec 15;41(12):1742-51. doi: 10.1086/498115. Epub. 2005 Nov 11.

May 2022

- Proctitis
- Lesions on the genital or perianal region alone
- MSM
- Sexual/intimate contact
- Likely to be seen in other communities
- Texas case: travel related, Dallas county

DSHS Confirms First Monkeypox Case in Texas for 2022

News Release

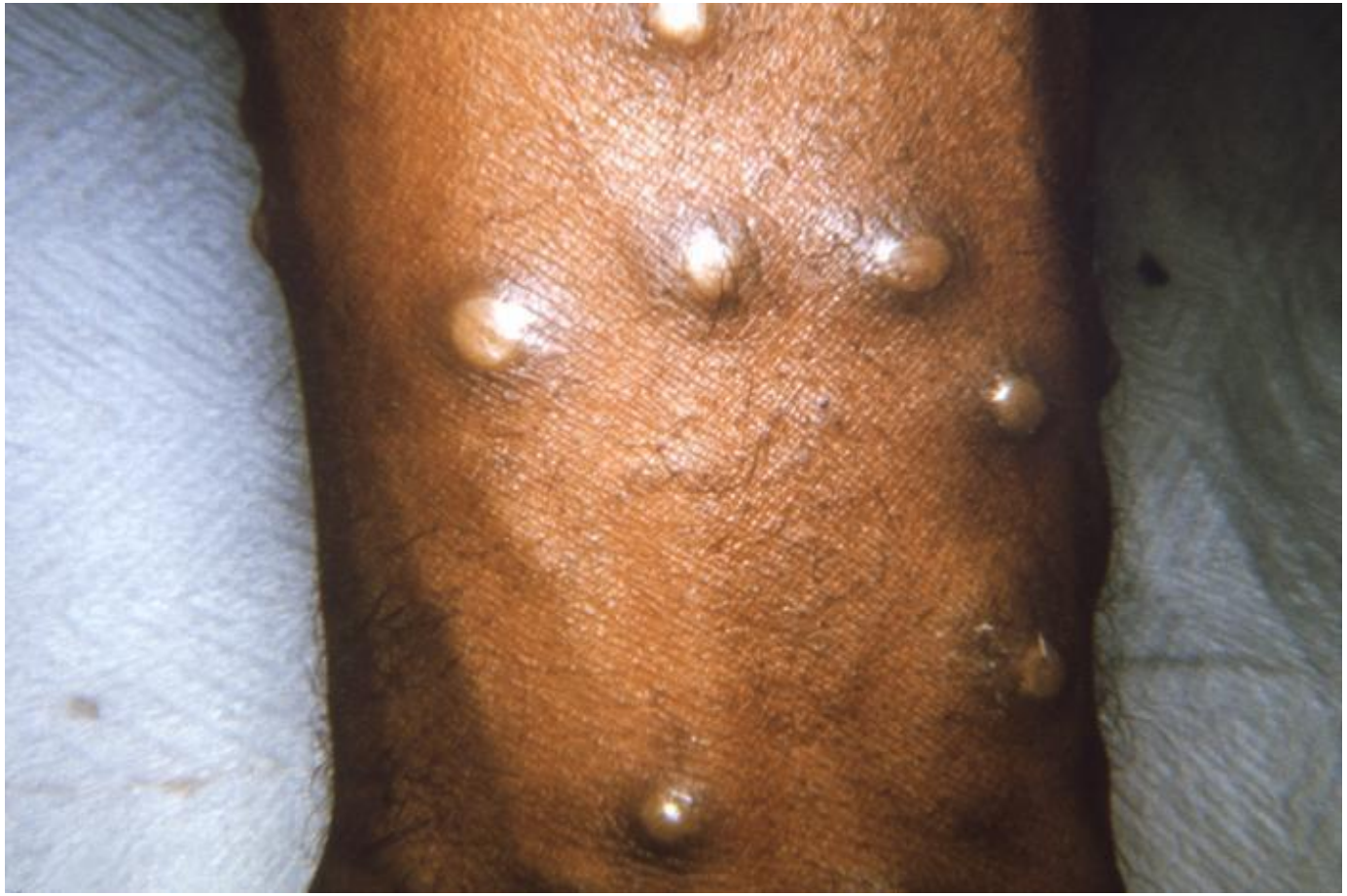
June 7, 2022

The Texas Department of State Health Services is working with Dallas County Health and Human Services and the Centers for Disease Control and Prevention to investigate a single case of monkeypox virus infection in a Dallas County resident with recent international travel. The patient is isolated at home. The public health investigation has identified a few people who may have been exposed in Dallas and are monitoring themselves for symptoms of infection. The illness does not currently present a risk to the general public.

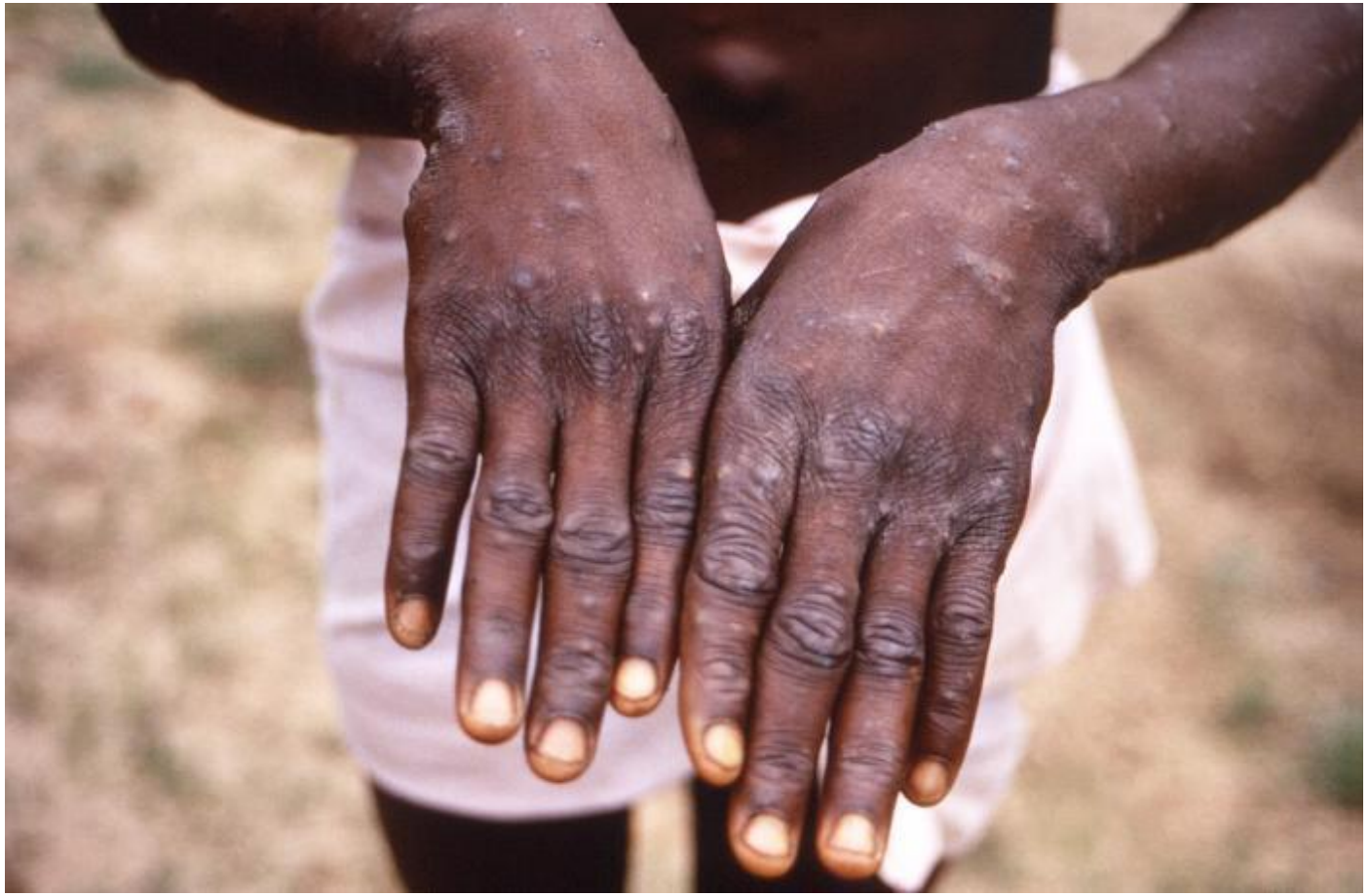
Public health officials are reaching out to passengers who could have been exposed to the patient on a flight from Mexico to Dallas with instructions on how to monitor themselves for symptoms.

The CDC are tracking multiple cases of monkeypox that have been reported in several countries that don't normally report monkeypox, including the United States. DSHS and the CDC urge health care providers in the U.S. to be alert for patients with rash illnesses consistent to monkeypox. More guidance for providers and general information about monkeypox is available online at www.dshs.texas.gov/IDCU/disease/Monkeypox.aspx and www.cdc.gov/poxvirus/monkeypox/response/2022/index.html.

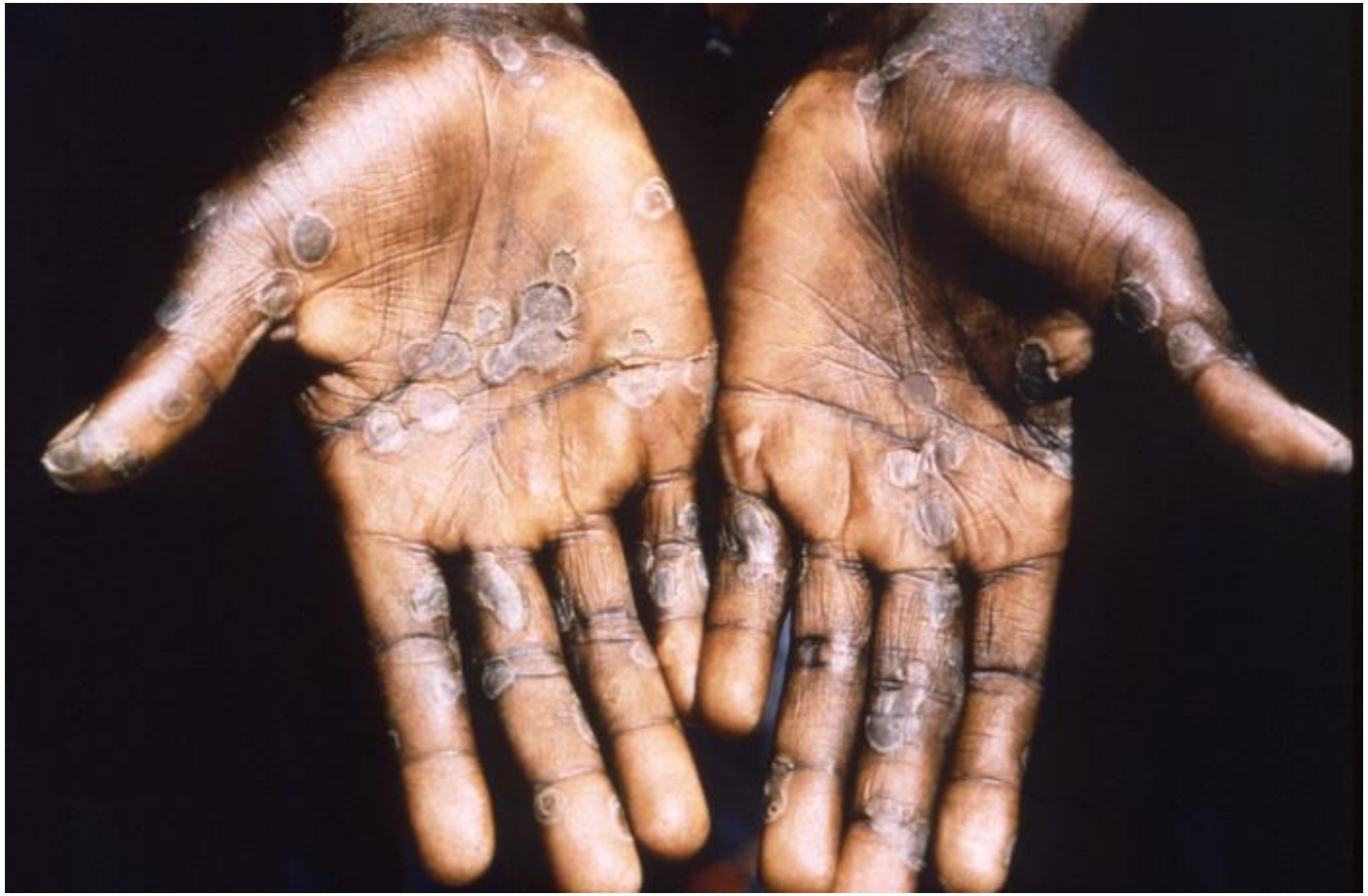
Monkeypox is transmitted to humans through close contact with an infected person or animal. It can also be transmitted from



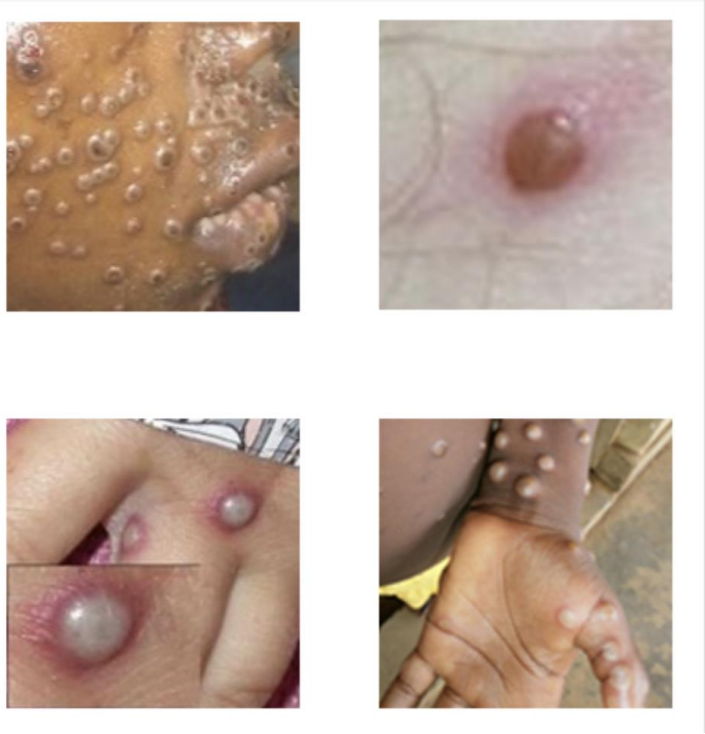
Pathology, Maculopapular lesions, arm, Smallpox Virus, Pustular phase, Variola major and minor. Contributed by Dr. John Noble, Jr., The Centers for Disease Control and Prevention (CDC)

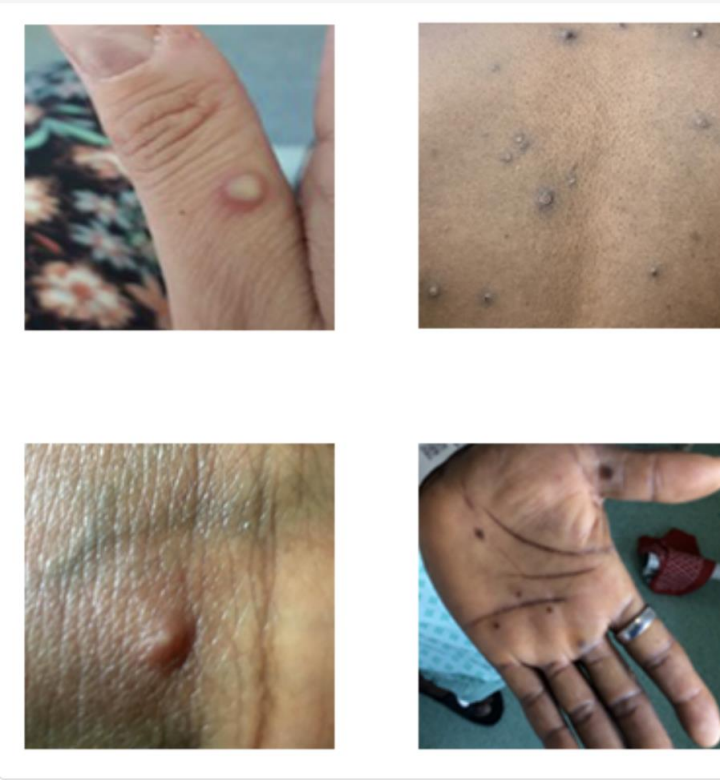


Monkeypox lesions on hands. Public Health Image Library #12763



Monkeypox lesions on palms. Public Health Image Library #12761



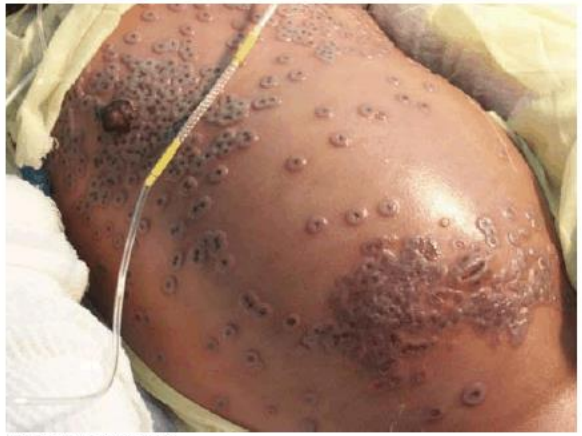


Varied appearance of lesions

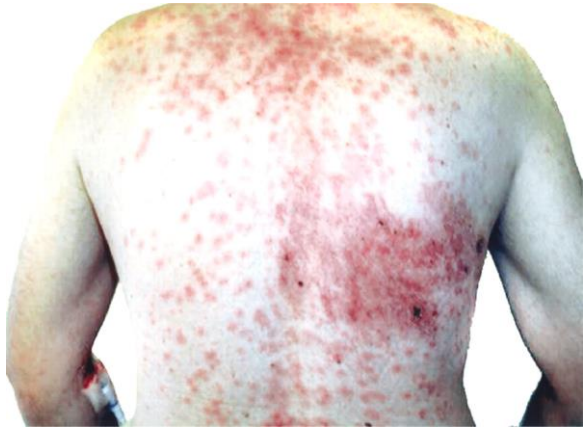
Differential Diagnosis

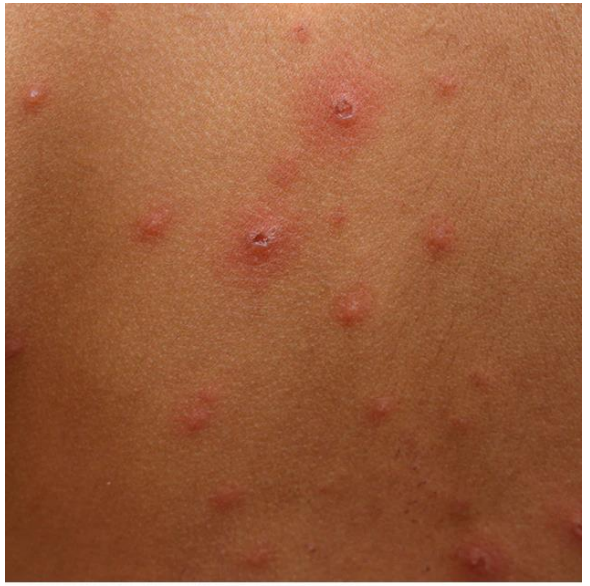
- Smallpox – symptom onset, timing of rash, distribution, less severe and lower fatality rate and scarring
- Generalized vaccinia
- Disseminated zoster
- Chickenpox – lesions more superficial, clusters, denser on trunk
- Mulloscum contagiosum
- Eczema herpeticum
- Disseminated herpes simplex
- Syphilis
- Yaws
- Anthrax
- Scabies
- Rickettsialpox
- Measles
- Bacterial skin infections
- Drug-associated eruption

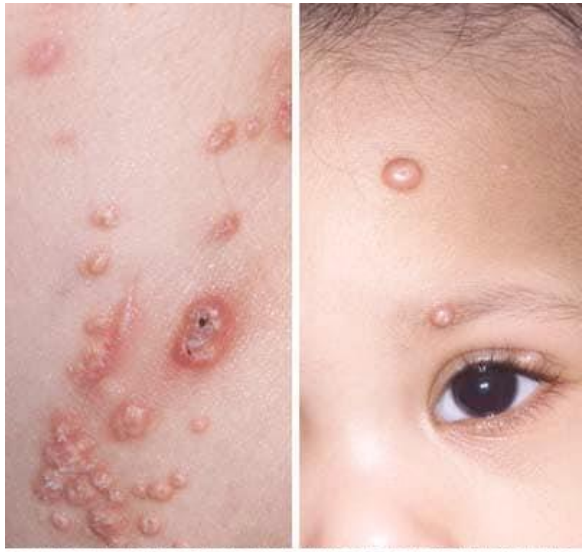
FIGURE. Abdomen and chest of a boy aged 28 months with a rash of umbilicated lesions caused by eczema vaccinatum — United States, 2007

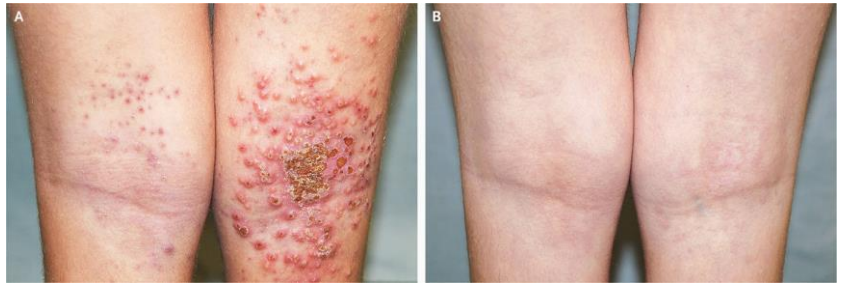


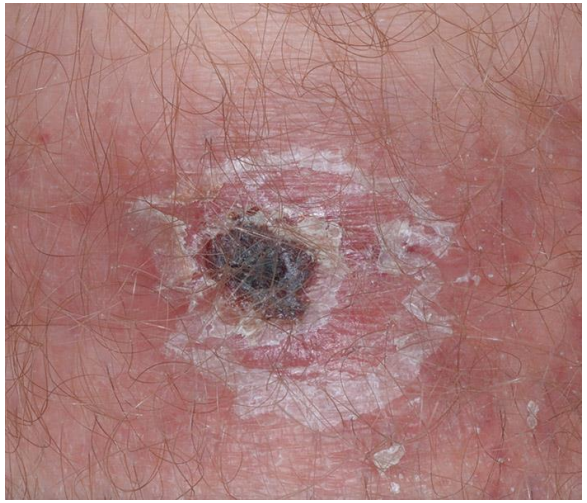
Photo/John Marcinak

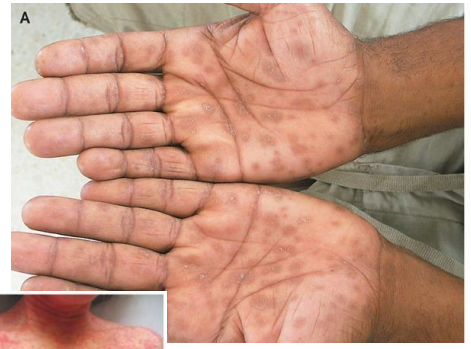


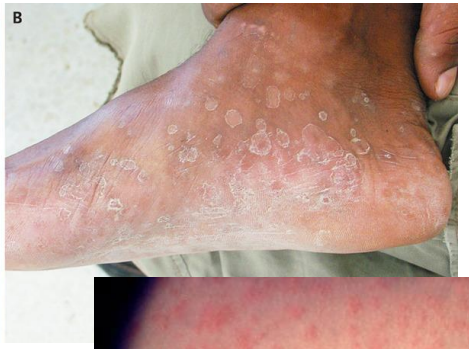


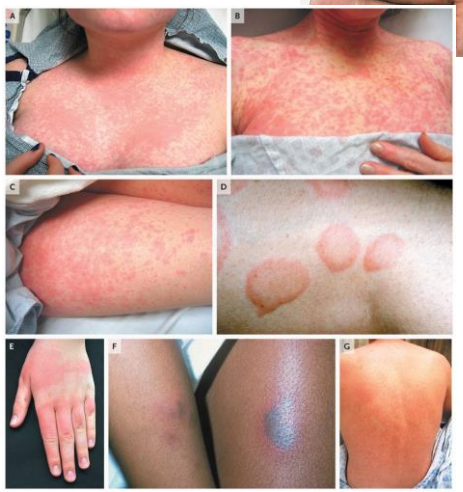


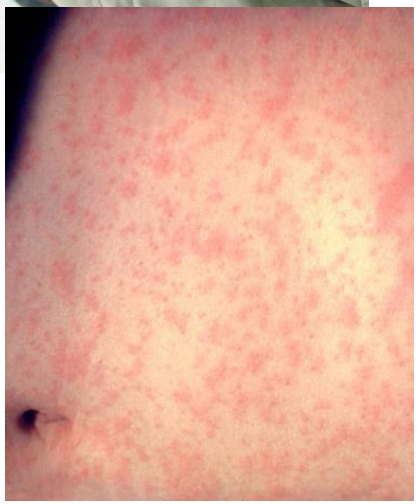












Key Characteristics

- Well circumscribed, deep seated, develop umbilication
- Same size and same stage of development on a single site of the body (ex: pustules on face or vesicles on legs)
- Fever *before* rash **although may not be true of current outbreak
- Lymphadenopathy
- Disseminated rash is centrifugal (more lesions on extremities, face)
- Palms, soles
- Painful until the healing phase when they become itchy

TABLE 132.1

Differential Diagnosis of Febrile Vesicular Pustular Rash Illnesses That May Be Confused With Smallpox

Modified from Centers for Disease Control and Prevention. Evaluating patients for smallpox: acute generalized vesicular or pustular rash illness protocol. https://www.cdc.gov/smallpox/clinicians/algorithm-protocol.html .

DISEASE	CLUES
Varicella	Most common in children younger than 10 years; children do not usually have a viral prodrome
Disseminated herpes zoster	Immunocompromised or elderly persons; rash looks like varicella, usually begins or erupts in dermatomal pattern
Impetigo *(Streptococcus pyogenes, Staphylococcus aureus)*	Honey-colored crusted plaques with bullae are classic but may begin as vesicles
Drug eruptions	Exposure to medications
Erythema multiforme minor	Target or bull's-eye lesions; often follows systemic viral infections such as herpes simplex virus; may include palms and soles
Erythema multiforme (including Stevens-Johnson syndrome)	Involves conjunctivae and mucous membranes
Enteroviral infections (especially hand-foot-and-mouth disease)	Seasonal—summer and fall
Disseminated herpes simplex virus	Similar to varicella
Scabies and insect bites	Pruritus; patient not febrile
Molluscum contagiosum	May disseminate in immunosuppressed individuals
Generalized vaccinia	History of vaccination with smallpox vaccine or contact with vaccinated individual
Monkeypox	Travel to endemic area; animal exposure

Diagnosis

- Until 2003 not detected outside of Africa
- CDC established case definition criteria
- Fewer healthcare providers have experience
- Vaccinated against smallpox – rash pleomorphic, not in uniform stage of development
- Serum antibodies detectable by time lesions appear

Case Definitions - 2022

Suspect Case

- New characteristic rash* **OR**
- Meets one of the epidemiologic criteria and has a high clinical suspicion† for monkeypox

Probable Case

- No suspicion of other recent *Orthopoxvirus* exposure (e.g., *Vaccinia virus* in ACAM2000 vaccination) **AND** demonstration of the presence of
  - *Orthopoxvirus* DNA by polymerase chain reaction of a clinical specimen **OR**
  - *Orthopoxvirus* using immunohistochemical or electron microscopy testing methods **OR**
- Demonstration of detectable levels of anti-orthopoxvirus IgM antibody during the period of 4 to 56 days after rash onset

Confirmed Case

- Demonstration of the presence of *Monkeypox virus* DNA by polymerase chain reaction testing or Next-Generation sequencing of a clinical specimen **OR** isolation of *Monkeypox virus* in culture from a clinical specimen

On This Page

Health Departments: If you have a patient that meets the probable or confirmed case definition, please contact the CDC Monkeypox Call Center at poxvirus@cdc.gov to report the case and obtain the case

Epidemiologic Criteria

Within 21 days of illness onset:

- Reports having contact with a person or people with a similar appearing rash or who received a diagnosis of confirmed or probable monkeypox **OR**
- Had close or intimate in-person contact with individuals in a social network experiencing monkeypox activity, this includes men who have sex with men (MSM) who meet partners through an online website, digital application ("app"), or social event (e.g., a bar or party) **OR**
- Traveled outside the US to a country with confirmed cases of monkeypox or where *Monkeypox virus* is endemic **OR**
- Had contact with a dead or live wild animal or exotic pet that is an African endemic species or used a product derived from such animals (e.g., game meat, creams, lotions, powders, etc.)

report the case and obtain the case report form.

A PDF version of the case report form data dictionary is available here [PDF - 3 MB] to preview only. Please do not attempt to fill out this PDF. Please contact the CDC Monkeypox Call Center to complete the case report form.

Exclusion Criteria

A case may be excluded as a suspect, probable, or confirmed case if:

- An alternative diagnosis* can fully explain the illness **OR**
- An individual with symptoms consistent with monkeypox does not develop a rash within 5 days of illness onset **OR**
- A case where high-quality specimens do not demonstrate the presence of *Orthopoxvirus* or *Monkeypox virus* or antibodies to orthopoxvirus

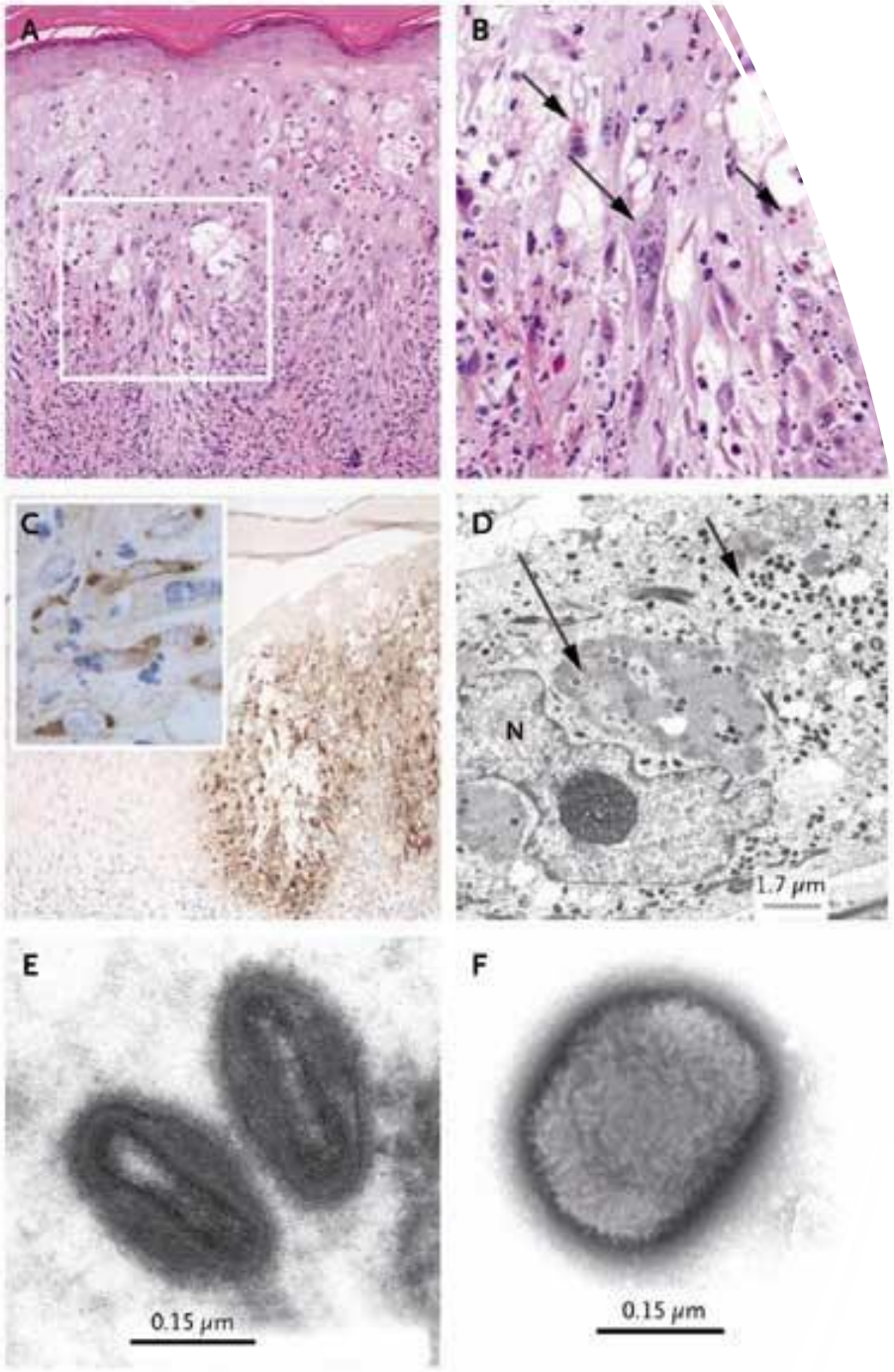
†Clinical suspicion may exist if presentation is consistent with illnesses confused with monkeypox (e.g., secondary syphilis, herpes, and varicella zoster).

*The characteristic rash associated with monkeypox lesions involve the following: deep-seated and well-circumscribed lesions, often with central umbilication; and lesion progression through specific sequential stages—macules, papules, vesicles, pustules, and scabs.; this can sometimes be confused with other diseases that are more commonly encountered in clinical practice (e.g., secondary syphilis, herpes, and varicella zoster). Historically, sporadic accounts of patients co-infected with *Monkeypox virus* and other infectious agents (e.g., varicella zoster, syphilis) have been reported, so patients with a characteristic rash should be considered for testing, even if other tests are positive.

Categorization may change as the investigation continues (e.g., a patient may go from suspect to probable).

Diagnosis

- Viral culture – oropharyngeal, nasopharyngeal swab, mammalian cell cultures only in specialized laboratories
- Specimens from skin lesions
- PCR for orthopoxvirus ->monkeypox DNA
- Visualization on EM, immunohistochemical staining for orthopoxvirus antigens, serum antibodies IgG and IgM (developed by CDC after 2003)
- Convalescent sera for specific antibodies IgM within 5 days, IgG within 8 days
- Histology and IHC – perivascular lympho-histiocytic infiltrate into the dermis, viral inclusions in keratinocytes
- Intracytoplasmic round to oval inclusions, sausage shaped structures centrally 200-300 um



Histopath

- Scattered degenerating and necrotic keratinocytes within the epidermis and a moderate inflammatory-cell infiltrate within the epidermis and superficial dermis
- Multinucleated cell (long arrow) and eosinophilic viral inclusion bodies (short arrows)
- Immunohistochemical staining of orthopoxvirus antigen within the epidermis. Inset shows immunoreactivity within individual keratinocytes
- Virions within the cytoplasm of a keratinocyte and includes immature forms that are being assembled (long arrow) and clusters of mature virions (short arrow).
- Virions with dumbbell-shaped cores characteristic of poxviruses.
- Negatively stained virion from cell culture

Prognosis

- Two clades of the virus
- West African – more favorable prognosis, case fatality rate <1%
- Central African – case fatality rate up to 11%
- Scarring, discoloration of skin, most patients recover within four weeks of symptom onset
- Previous vaccination status, health status, concurrent illnesses, comorbidities

Complications

- Secondary bacterial infection
- Permanent scarring
- Hyperpigmentation or hypopigmentation
- Permanent corneal scarring -> vision loss
- Pneumonia, respiratory failure
- Dehydration (vomiting, diarrhea, decreased oral intake due to painful oral lesions, and insensible fluid loss from widespread skin disruption)
- Sepsis
- Encephalitis
- Death

Treatment

- Mild, self-limiting disease, supportive care
- Consider for treatment with severe disease or at risk of severe disease
  - Hemorrhagic disease, confluent lesions, sepsis, encephalitis, secondary skin infection, severe GI symptoms, bronchopneumonia
  - Immunocompromised – HIV/AIDS, leukemia, lymphoma, malignancy, SOT, tx with alkylating agents, antimetabolites, radiation, TNF inhibitors, high dose steroids, HSCT, autoimmune disease
  - Pediatric patients, less than age 8, pregnant, breastfeeding women
  - Infection in "high risk" areas eyes, mouth, genitals, anus

Treatment

- No specific treatment approved, use of smallpox tx agents
- Tecovirimat (TPOXX) - antiviral, intracellular viral release inhibitor, FDA approved, human smallpox adults and children over 3 kg, Expanded Access Investigational New Drug Protocol allows for use outside of smallpox
  - https://www.cdc.gov/poxvirus/monkeypox/clinicians/obtaining-tecovirimat.html
- Cidofovir – antiviral, FDA approved for CMV in AIDS, also EA-IND
- Vaccinia Immune Globulin IV – licensed by FDA for tx of complications due to vaccinia vaccination, EA-IND
- Brincidofovir – antiviral, DNA polymerase inhibitor, oral, FDA approved for tx smallpox adult and ped patients, including neonates, not currently under EA-IND
- Unknown efficacy against Monkeypox

Vaccination

- Orthopoxvirus species share genetic, antigenic features
- Cross-protection with infection or vaccination
- Vaccination with vaccinia virus protects against variola, monkey, and cowpox
- Neutralizing antibody production
- Smallpox vaccinations discontinued in 1978
- Immunity has waned

Pre-exposure ppx

- ACIP recommends jobs at high risk of exposure – lab personnel who perform testing to diagnose orthopoxviruses, research lab workers directly handling cultures, animals, certain HCW and public health response team members for preparedness, anticipate caring for patients
- At this time, most clinicians and labs not performing these functions are not advised to get pre-exposure ppx

Table 1. Vaccination Strategies Used in the 2022 U.S. Monkeypox Outbreak

Strategy	Definition	Criteria
Post-Exposure Prophylaxis (PEP)	Vaccination **after known exposure** to monkeypox	• People who are known contacts to someone with monkeypox who are identified by public health authorities, for example via case investigation, contact tracing, or risk exposure assessment
Expanded Post-Exposure Prophylaxis (PEP++)	Vaccination **after known or presumed** exposure to monkeypox	Any of the following: • People who are known contacts to someone with monkeypox who are identified by public health authorities, for example via case investigation, contact tracing, or risk exposure assessment • People who are aware that a recent sex partner within the past 14 days was diagnosed with monkeypox • Certain gay, bisexual, or other men who have sex with men, or transgender and gender diverse people who have sex with men, who have had any of the following within the past 14 days: sex with multiple partners (or group sex); sex at a commercial sex venue; or sex in association with an event, venue, or defined geographic area where monkeypox transmission is occurring
Pre-Exposure Prophylaxis (PrEP)	Vaccination **before exposure** to monkeypox	• People in certain occupational risk groups*

PRIORITY GROUPS

The JYNNEOS™ vaccine, which is proven to prevent Monkeypox and is FDA approved, is available in limited quantities for those who meet the following criteria:

VACCINE ELIGIBILITY PRIORITY GROUPS

Priority Group 1

- Exposed individuals identified through contact tracing

Priority Group 2

Individuals with presumed exposure who:

- Know that a sexual partner in the past 14 days was diagnosed with monkeypox
- Attended an event or venue in the past 14 days and had a high-risk of exposure to someone with confirmed monkeypox through skin-to-skin or sexual contact
- Have a sex partner who is showing symptoms of monkeypox, such as rash or sores

Priority Group 3

- People living with HIV
- People on PrEP for the prevention of HIV
- Men (*cisgender and transgender*) and transwomen who have sex with men who have had multiple or anonymous sex partners within the previous 21 days

For Priority Group 3 – during low vaccine availability the following can be further prioritized:

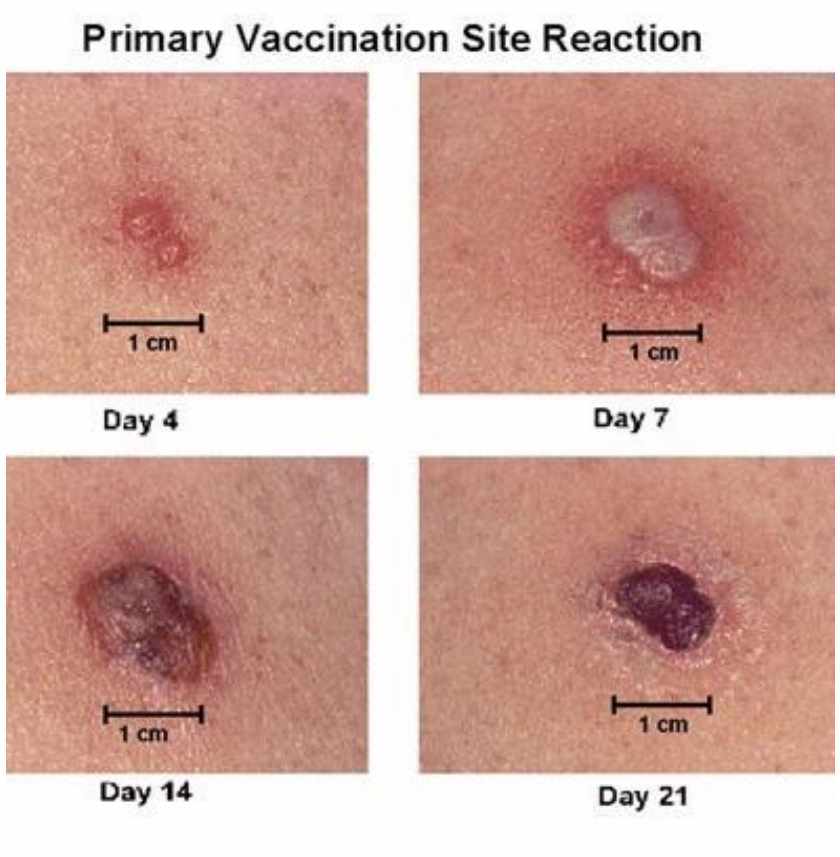
- have had a diagnosis of early syphilis, gonorrhea, or chlamydia within the previous 12 months
- have a condition that may increase their risk for severe disease if infected with monkeypox virus, such as atopic dermatitis or eczema

NOTE: Vaccines for Priority Group 3 are available from select healthcare providers by appointment and only to those who meet the criteria listed above and have not had monkeypox symptoms. Please check with your healthcare provider to see if they have vaccines available.

Adequate vaccine supply to vaccinate everyone who meets vaccine eligibility is not currently available. We are working with our local, state, and federal officials to procure more and will expand our current eligibility criteria if/when we receive more.

ACAM200

- Live Vaccinia virus
- Inoculated by pricking skin surface, lesion will develop at site (the "take")
- Can spread to other people or sites
- Precautions to prevent spread of vaccine virus
- Considered vaccinated within 28 days



https://www.cdc.gov/smallpox/vaccine-basics/who-gets-vaccination.html

Jynneos

- Replication defective, modified vaccinia virus
- Two shot series, four weeks apart
- Superior safety profile compared to 1st and 2nd generation smallpox vaccines
- Does not create skin lesion or pose risk of local/disseminated disease (vs live vaccinia virus preparations)
- Safe, stimulates antibody production in patients with atopy, immunocompromised (contra-indication for the live vaccinia virus preparations)
- Not considered vaccinated until 2 weeks after the second dose

Post-exposure

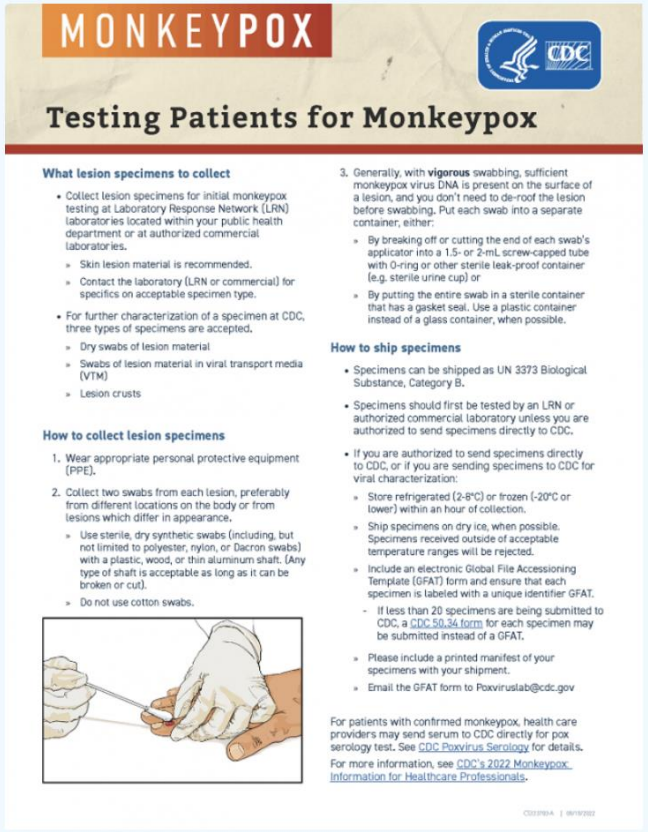
- High-risk exposure: contact between broken skin or mucous membranes, infected patient's body fluids, respiratory droplets, scabs warrants post-exposure vaccination ASAP
- Vaccination within 4 days of exposure may prevent disease onset, within 14 may reduce severity
- Revaccination after exposure: vaccination > 3 years should consider

CDC Infection Control

- Isolation, single person room, closed door
- Standard, contact, and droplet precautions, PPE: gown, gloves, eye protection, N-95
- Escalation to airborne precautions, if possible (high risk procedures – intubation, bronch)
- Post-exposure: monitor temp, symptoms twice daily for 21 days
- Infectiousness aligns with symptom onset – close contacts need not be isolated if no symptoms

Who to call…

- Possible cases – report to local hospital epi, infection control personnel
- Contact of local health department – SA Metro Health with testing for orthopoxvirus, if positive sent to CDC to confirm
- Contact of CDC
- Alert laboratory personnel
- Specimen collection, PPE (gown, gloves, eye protection, N95)
- RT-PCR on lesion material, more than one should be sampled, different parts of body
- Home | Submitting Specimens to CDC | Infectious Diseases Laboratories | CDC



MONKEYPOX

Testing Patients for Monkeypox

What lesion specimens to collect

- Collect lesion specimens for initial monkeypox testing at Laboratory Response Network (LRN) laboratories located within your public health department or at authorized commercial laboratories.
  - Skin lesion material is recommended.
  - Contact the laboratory (LRN or commercial) for specifics on acceptable specimen type.
- For further characterization of a specimen at CDC, three types of specimens are accepted.
  - Dry swabs of lesion material
  - Swabs of lesion material in viral transport media (VTM)
  - Lesion crusts

How to collect lesion specimens

1. Wear appropriate personal protective equipment (PPE).
2. Collect two swabs from each lesion, preferably from different locations on the body or from lesions which differ in appearance.
   - Use sterile, dry synthetic swabs (including, but not limited to polyester, nylon, or Dacron swabs) with a plastic, wood, or thin aluminum shaft. (Any type of shaft is acceptable as long as it can be broken or cut).
   - Do not use cotton swabs.

3. Generally, with **vigorous** swabbing, sufficient monkeypox virus DNA is present on the surface of a lesion, and you don't need to de-roof the lesion before swabbing. Put each swab into a separate container, either:
   - By breaking off or cutting the end of each swab's applicator into a 1.5- or 2-mL screw-capped tube with O-ring or other sterile leak-proof container (e.g. sterile urine cup) or
   - By putting the entire swab in a sterile container that has a gasket seal. Use a plastic container instead of a glass container, when possible.

How to ship specimens

- Specimens can be shipped as UN 3373 Biological Substance, Category B.
- Specimens should first be tested by an LRN or authorized commercial laboratory unless you are authorized to send specimens directly to CDC.
- If you are authorized to send specimens directly to CDC, or if you are sending specimens to CDC for viral characterization:
  - Store refrigerated (2-8°C) or frozen (-20°C or lower) within an hour of collection.
  - Ship specimens on dry ice, when possible. Specimens received outside of acceptable temperature ranges will be rejected.
  - Include an electronic Global File Accessioning Template (GFAT) form and ensure that each specimen is labeled with a unique identifier GFAT.
    - If less than 20 specimens are being submitted to CDC, a CDC 50.34 form for each specimen may be submitted instead of a GFAT.
  - Please include a printed manifest of your specimens with your shipment.
  - Email the GFAT form to Poxviruslab@cdc.gov

For patients with confirmed monkeypox, health care providers may send serum to CDC directly for pox serology test. See CDC Poxvirus Serology for details.

For more information, see CDC's 2022 Monkeypox: Information for Healthcare Professionals.

PRINTOUT

Testing Patients for Monkeypox

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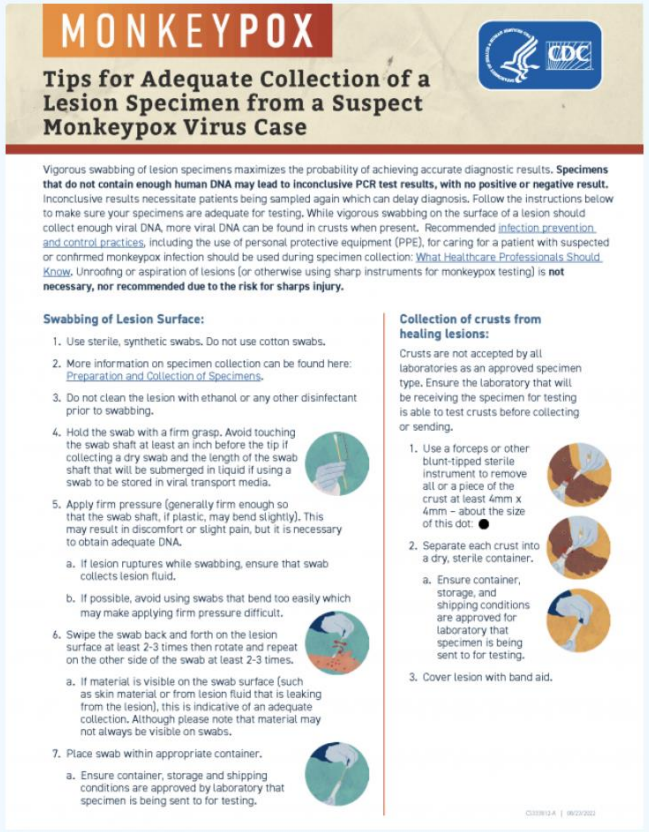

MONKEYPOX

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.

PRINTOUT

Tips For Adequate Collection of a Lesion Specimen From a Suspect Monkeypox Virus Case

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Duration of Isolation

- Isolation at home for the duration of illness
- Spread from the time symptoms start until all symptoms have resolved, including full healing of the rash with formation of a fresh layer of skin. Typically lasts two to four weeks.
- Symptomatic with fever or any respiratory symptoms: remain isolated in the home and away from others unless it is necessary to see a healthcare provider or for an emergency.
- While a rash persists but in the absence of a fever or respiratory symptoms: Cover all parts of the rash, wear a well-fitting mask

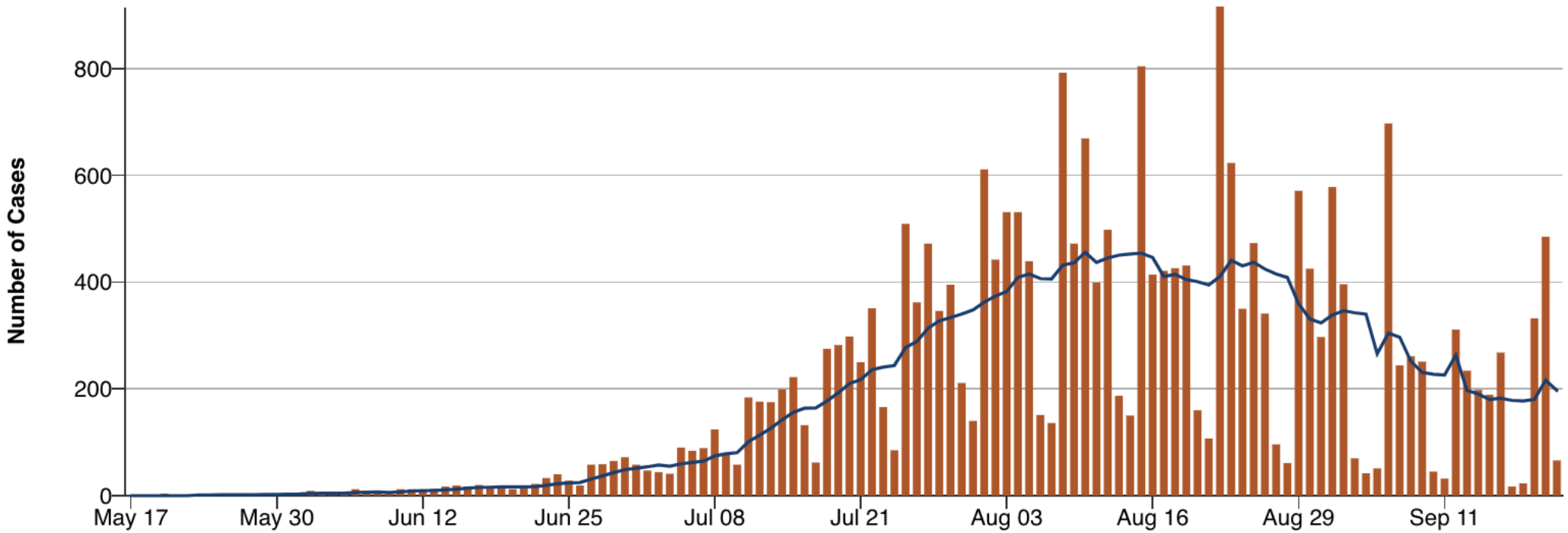
Emerging guidance

- Transmission - brief interactions, in proximity and for a long duration unlikely to spread monkeypox
- Direct skin-to-skin contact, including sexual and/or close intimate contact, identified as a predominant type of exposure
- Most people with monkeypox have been adults and have not required hospitalization
- Deaths have occurred but are rare

Monkeypox + HIV

- Large proportion of monkeypox cases – persons living with HIV (PLWH)
- CDC MMWR: 2000 cases, nearly 40%, European CDC and WHO similar stats
- Outbreak concentrated among MSM, a population already at risk for HIV – alone does not explain the high rate
- Sexual networks, not necessarily the HIV status, recent hx of other STIs – overlapping risk factors
- HIV effect on the immune system - HIV negative vs. HIV co-infected – PLWH more prolonged illness, larger lesions >2 cm, higher rates of both secondary bacterial skin infections and genital ulcers
- HIV patients may see doctors more often – cases are more readily identified

Daily Monkeypox Cases Reported* and 7 Day Daily Average



https://www.cdc.gov/poxvirus/monkeypox/response/2022/mpx-trends.html

Lessons Learned from COVID and HIV

- Early 2020 – major errors in developing a test, mistakes in design, manufacturing, FDA initially refusing to allow labs develop, use own COVID-19 tests
- Monkeypox – lack of easy testing, surveillance size of outbreak difficult to estimate
- Patient sees healthcare provider -> contact state/local health department, CDC lab partner runs generic orthopoxvirus testing on sample -> if positive, goes to CDC in Atlanta to test for monkeypox

Areas for improvement

- Centralization of testing – wasting time, limit capacity of testing
- Testing based on PCR – lots of labs can develop/perform, can be validated
- Increasing the testing capacity even before widespread testing needed (low-cost vs risk)
- Release of monkeypox testing protocols from CDC – other labs can develop/run testing, guidance by FDA
- In contrast to COVID-19, vaccines, FDA approved antivirals (recent close contact, vaccinating exposed "ring vaccination")

Questions?

- Thank you!

References

- Petersen BW, Harms TJ, Reynolds MG, Harrison LH. Use of Vaccinia Virus Smallpox Vaccine in Laboratory and Health Care Personnel at Risk for Occupational Exposure to Orthopoxviruses — Recommendations of the Advisory Committee on Immunization Practices (ACIP), 2015. MMWR Morb Mortal Wkly Rep 2016;65:257–262. DOI: http://dx.doi.org/10.15585/mmwr.mm6510a2
- Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, Zumla A. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect Dis Clin North Am. 2019 Dec;33(4):1027-1043. doi: 10.1016/j.idc.2019.03.001. Epub 2019 Apr 11. PMID: 30981594.
- Jezek Z, Szczeniowski M, Paluku KM, Mutombo M. Human monkeypox: clinical features of 282 patients. J Infect Dis. 1987 Aug;156(2):293-8. doi: 10.1093/infdis/156.2.293. PMID: 3036967.
- Cono J, Cragan JD, Jamieson DJ, Rasmussen SA. Prophylaxis and treatment of pregnant women for emerging infections and bioterrorism emergencies. Emerg Infect Dis. 2006 Nov;12(11):1631-7. doi: 10.3201/eid1211.060618. PMID: 17283610; PMCID: PMC3372351. Mbala PK, Huggins JW, Riu-Rovira T, Ahuka SM, Mulembakani P, Rimoin AW, Martin JW, Muyembe JT. Maternal and Fetal Outcomes Among Pregnant Women With Human Monkeypox Infection in the Democratic Republic of Congo. J Infect Dis. 2017 Oct 17;216(7):824-828. doi: 10.1093/infdis/jix260. PMID: 29029147.
- Ogoina D, Iroezindu M, James HI, Oladokun R, Yinka-Ogunleye A, Wakama P, Otike-Odibi B, Usman LM, Obazee E, Aruna O, Ihekweazu C. Clinical Course and Outcome of Human Monkeypox in Nigeria. Clin Infect Dis. 2020 Nov 5;71(8):e210-e214. doi: 10.1093/cid/ciaa143. PMID: 32052029.
- Moore M, Zahra F. Monkeypox. 2022 May 22. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 34662033.
- Huhn GD, Bauer AM, Yorita K, Graham MB, Sejvar J, Likos A, Damon IK, Reynolds MG, Kuehnert MJ. Clinical characteristics of human monkeypox, and risk factors for severe disease. Clin Infect Dis. 2005 Dec 15;41(12):1742-51. doi: 10.1086/498115. Epub 2005 Nov 11. PMID: 16288398.
- Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases, 132, 1809-1817.e3
- Monkeypox | Poxvirus | CDC
- Monkeypox (who.int)
- Monkeypox: experts give virus variants new names (who.int)