Mpox

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Introduction

- Monkeypox is a viral zoonosis (Orthopoxyvirus) that occurs in the rainforest of Central and Western Africa.
  - First identified as cause of a pox outbreak in DRC in 1970s.
  - Two strains exist, one from Central Africa – Clade 1 (rarer) and a milder strain from Western Africa - Clade 2 (most outbreaks).
  - First described in 1950 from a colony of sick monkeys.
- It causes a clinical illness similar to Smallpox, though milder, less transmissible, and with a lower mortality.
- Outbreaks have increased over the past 20 years, 20x.
  - Waning smallpox immunity in Africa and elsewhere.
    - Unvaccinated 5X more likely to get infected.
  - Increased human interaction to animals (climate change).

Epidemiology

- Reservoir is unknown.
  - Likely small mammals that live in Rainforest (rodents).
  - Forest monkeys also noted to be infected.
- First reported in humans in 1970's; all cases up to 2003 in Africans exposed to infected animals in the rainforest.
  - First outbreak outside of Africa – US 2003 (from exposure to prairie dogs housed next to African rodents prior to purchase).
  - Sporadic outbreaks since then, linked to Africa travel (forest).
- In 2022, a worldwide outbreak occurred which primarily affected MSM (98% of all cases), Clade 2b. Up to 30-40% HIV+. Those with CD<200 →higher risk for severe dis.
- 2024 is seeing another large outbreak in DRC, Clade 1a.

Epidemiology

- WHO stopped vaccinating against smallpox in 1980, and in a surveillance study between 2005-2007, the WHO found a 20% increase in incidence, with 760 lab confirmed cases identified.
- There were no cases in Nigeria from late 1970's until 2017. Since 2017, Nigeria has seen outbreaks, as have DRC, Rep of Congo, Gabon, Ghana, Ivory Coast, Liberia, Sierra Leone, and South Sudan.
- Younger individuals have higher risk due to lack of any immunity from prior smallpox vaccine.
- Vaccine effect wanes of time – 18% of Spanish Mpox patients had history of prior smallpox vaccination.

2022 Outbreak

- Spread primarily among MSM
  - Many were HIV positive.
- By Aug 2022, there were 1000 new cases per day, and by Oct 2022, 75,885 global cases reported.
  - 99% male, 94% reported male to male intimate contact
- Death rate was low (Clade 2).
- This outbreak had Mpox present primarily as an STI, with genital lesions and local complications.
- CD4<200 associated with higher risk for severe disease.

Current Outbreak

- Cases of Mpox have been steadily increasing in DRC for the past decade.
- Since Jan 2023, DRC has reported 27,000 cases and over 1,300 deaths (4.8% mortality rate), mostly in children.
- In 2024, 90% of cases have occurred in DRC – over 18,000 cases (>3000 lab confirmed) and over 615 deaths. Largest outbreak on record.
  - 2/3 occurred in children / 50% new cases in South Kivu Province.
  - Affecting surrounding countries, including Burundi, CAR, Rep of Congo, Rwanda, Uganda, among others.
    - Burundi, Rwanda and Uganda are not considered endemic.
- On 8/14/24, the WHO declared the outbreak a Public Health Emergency of International Concern.

DRC

- There are several simultaneous outbreaks, occurring in Kinshasa and other large cities, and in multiple provinces across the country.
  - Transmission has occurred in typical ways – via contact with live or dead wild animals, through household transmission, through patient care, or through sexual contact, particularly among MSM and female sex workers and their contacts.
  - Most cases have occurred in children <15 years of age.

Transmission

- Mpox is a zoonosis; primary transmission is animal to human.
  - Contact with animal bodily fluids, often via bite or scratch.
  - Handling infected animal or cleaning cage may also transmit
    - Degree of exposure affects disease severity.
- Humans may transmit to other humans.
  - Human to human: occurs via direct contact with infected sores.
    - Exposure to skin lesions via close contact or linens.
    - Close contact with body fluids – directly touching body fluid or sore, then one's mucus membrane or breach in skin.
      - Sexual transmission / stroking / hugging / kissing. Found in semen.
    - Can cross placenta and cause fetal infection and death.
    - Respiratory transmission may occur rarely if at all.

Period of Infectivity

- Patients are generally infectious from onset of rash until all lesions have scabbed over and re-epithelialized.
  - Viral shedding from symptom onset to viral clearance was ~ 40 days in 90% of cases in 2022 study.
    - Longer in immunocompromised (AIDS).
- However, viral shedding may sometimes occur 1-4 days prior to symptoms.
- Skin lesions have highest amounts of viral DNA, so are most infectious, compared to blood, urine, semen and mucus membranes.

Infection Type / Pathogenesis

- Localized (at site of viral entry) vs systemic (diffuse rash and viremia).
- Typically, during African outbreaks, most infected patients that present for care have a systemic illness.
  - 90% with fever.
- During 2022-23 global outbreak, however, many patients did not have systemic disease; only localized genital, anal, oral disease, at site of inoculation.

High Risk Patients

- Underlying immunodeficiency, such as HIV.
  - Those with well controlled HIV or with preserved CD4 counts, tend to do well.
- Young children with Clade 1 virus tend to do most poorly and have highest mortality rates, compared to immunocompetent adults.
- Pregnant women.
- Those presenting with mucosal disease or end-organ involvement.

Incubation Period

- Incubation is 5-13 days.
  - Range is 4-21 days.
- May depends on exposure type
  - Degree of contact: the more significant the exposure (animal scratch or bite), the shorter the incubation, and the more likely invasive disease will occur.
  - Smallpox immunity status likely also plays a role
- Usually, symptoms develop during the 2nd week after exposure.
- Illness lasts 2-4 weeks.

Clinical Manifestations

- Systemic illness: fever, myalgias, h/a, sore throat, fatigue, LAD.
  - LAD is a distinguishing feature from smallpox or chicken pox.
    - Disease may be generalized or focal.
  - Systemic symptoms generally lasts 1-5 days.
  - 1-3 days after fever starts, RASH occurs
    - During 2022 outbreak, rash often showed up before or without fever.
- Rash may last 2-3 weeks.
  - CDC recommends that return to work only occur when new skin forms over scabbed areas.
- Secondary bacterial infection may occur, as well as complication from mucosal lesions, which may result in severe fibrosis.
- Mortality: West African Strain (Clade 2): <1%.

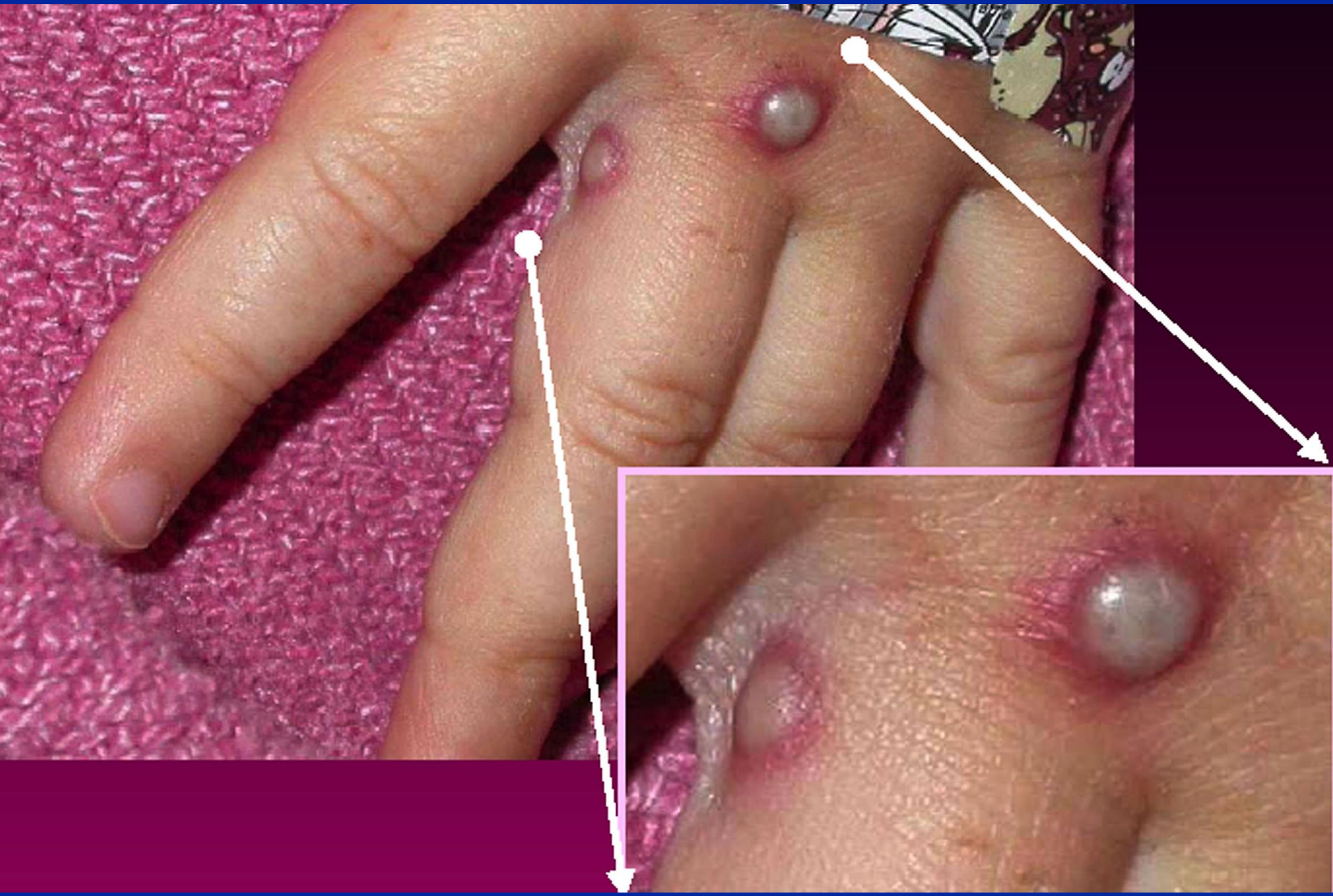
  Congo Strain (Clade 1): 3-4% (current outbreak)

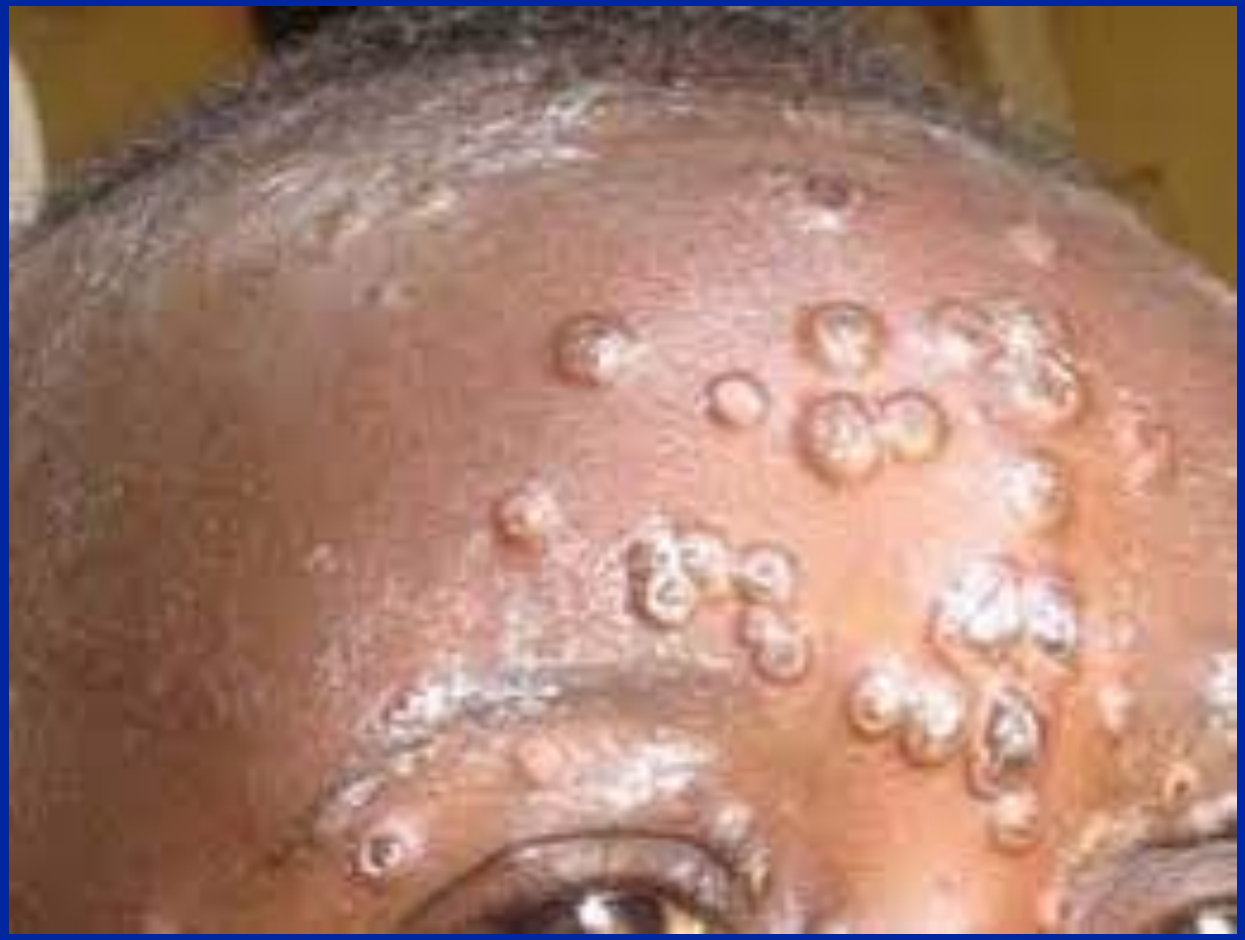
The Rash

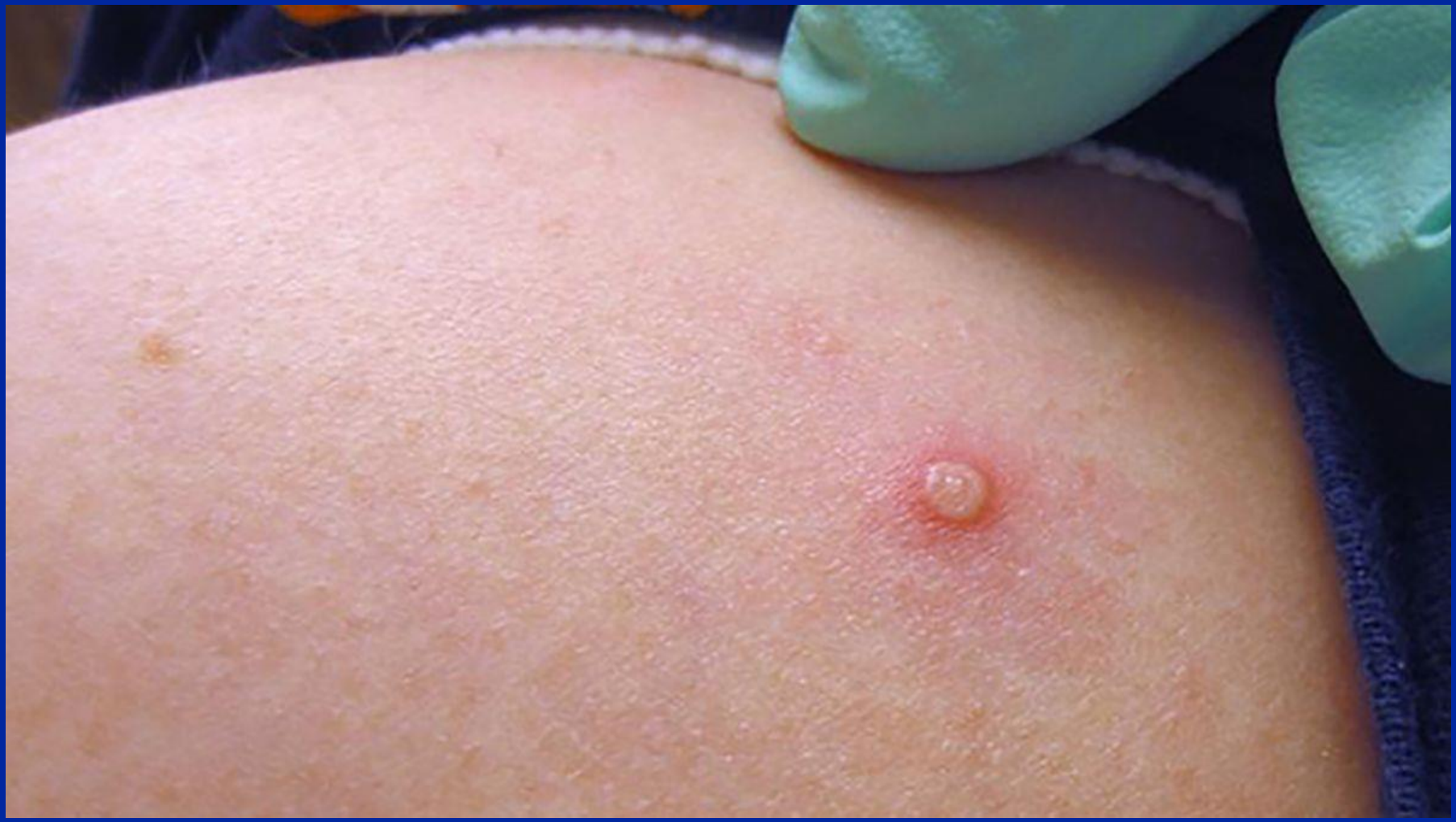
- Starts centrally (head/face) and spreads out (centrifugal spread).
  - More lesions on extremities and face than on trunk.
- Progresses through 4 stages: macules, papules, vesicles, pustules, before eventually scabbing over and eventually healing.
  - Umbilication is very common.
  - Well circumscribed, firm, often painful.
  - During global outbreak, many patients presented focally, with lesions primarily in oral, genital or anorectal areas. Proctitis, rectal bleeding, penile and pelvic lesions and mucosal involvement have all been reported.
- Lesions are similar size and stage on single body site – may have vesicles on face and pustules on arms.
  - Palms, soles and mucus membranes are frequently involved.
- Many of the Elmhurst cases had had focal genital rash that had many lesions, and sparse diffuse rash. Others were diffuse.

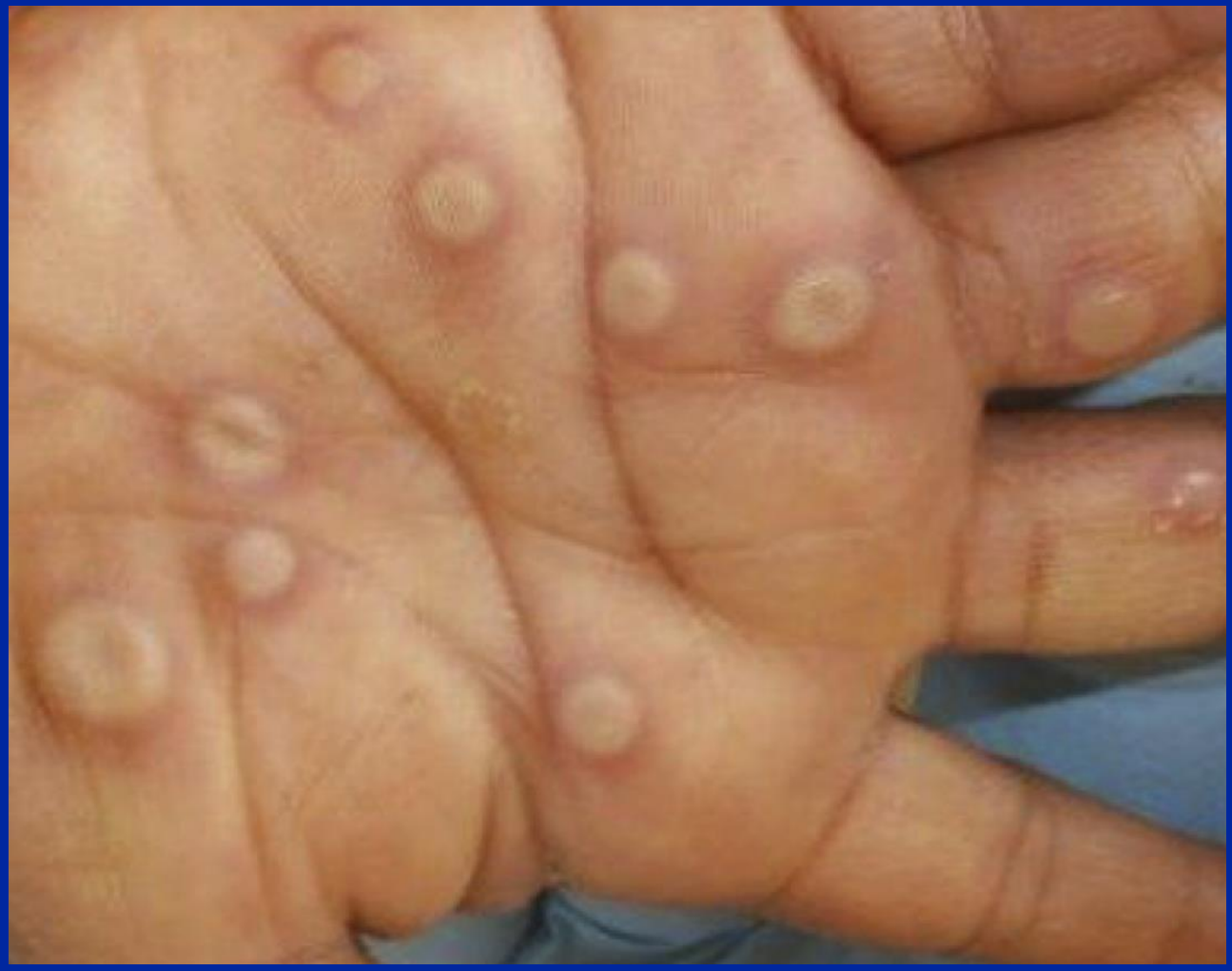
Other Findings

- Ocular involvement – conjunctivitis, periorbital cellulitis, keratitis, vision loss.
- Neurologic involvement – encephalitis / encephalomyelitis.
  - May have positive PCR in CSF.
- Pulmonary involvement – pneumonitis or nodular infiltrates, in the immunocompromised.







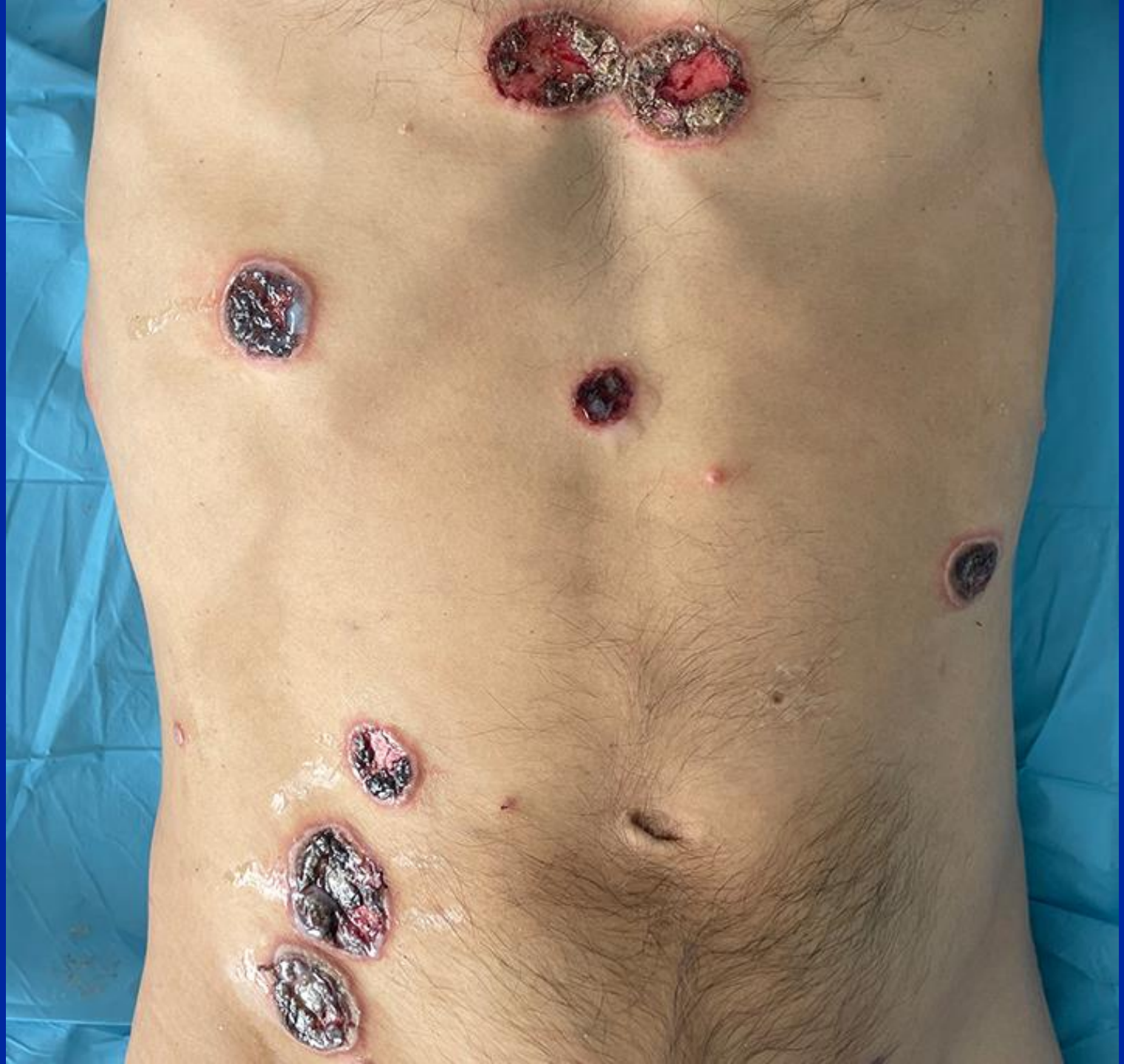


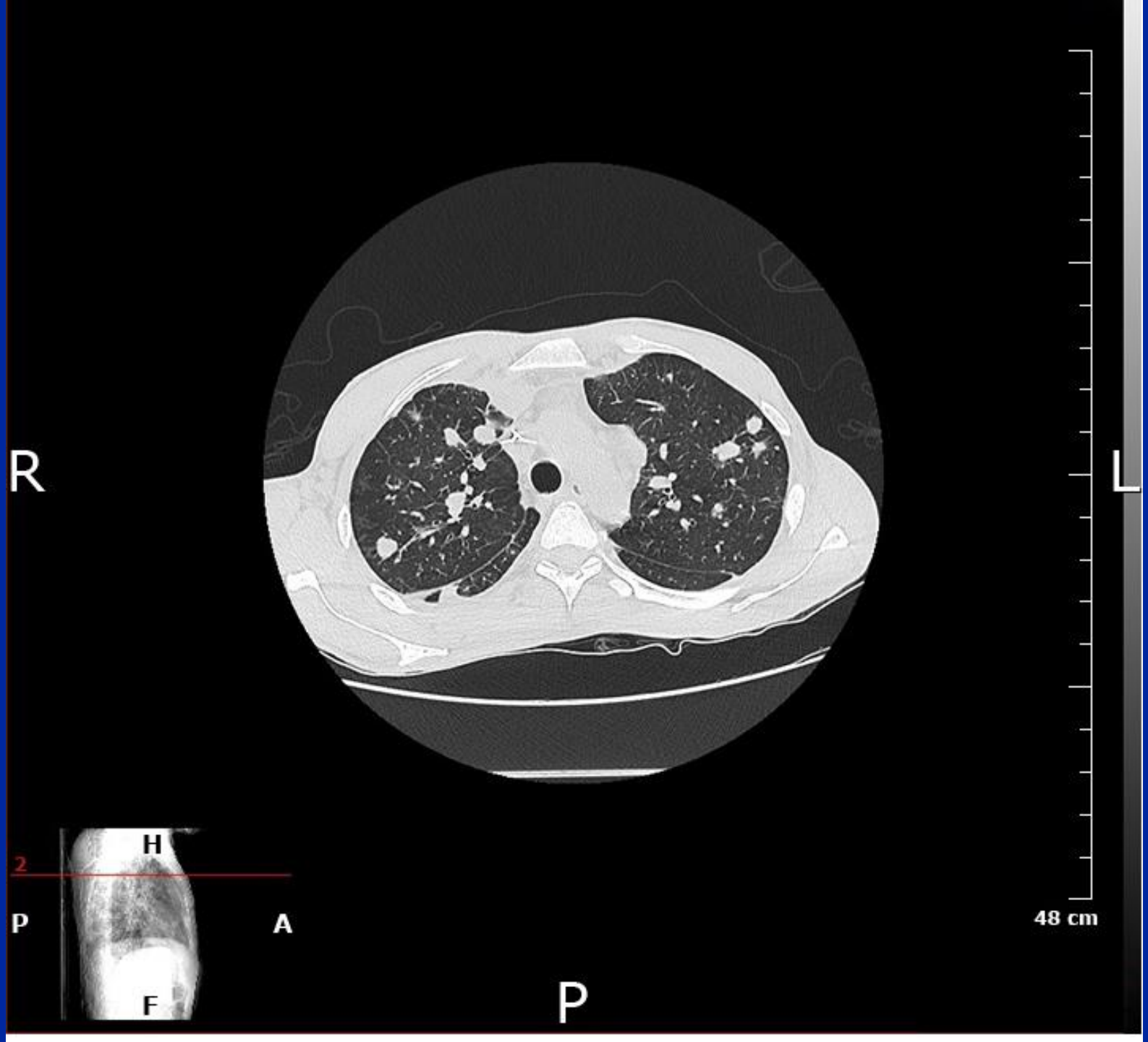
Physical Exam

- Do thorough skin and mucosal exam, including anogenital area and its mucosal surfaces.
- Look for characteristic rash.
  - Vesicular rash with umbilication.
- Rash concentrated in face, arms, legs.
- Genital areas may be more heavily involved in sexually transmitted cases, but skin may have light diffuse rash as well.
- Assess for ocular, mucosal, neuro involvement.

Advanced HIV and Mpox

- Advanced AIDS patients are more likely to have severe disease, and very protracted illness.
  - Patients with advanced, uncontrolled HIV (CD4 <50) have been noted to have extremely prolonged illnesses, resulting in many of the deaths seen in Clade 2 outbreaks.
  - One study of 382 HIV patients with CD<350, 107 (28%) needed hospitalization, and 27 (7%) died.
    - Deaths all occurred in patients with Advanced AIDS – CD4 <200 cells.
    - Some AIDS patients developed large necrotic skin lesions, while others had lung involvement with nodular infiltrates.
    - Immune reconstitution may occur if they start or restart ARV.

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When to suspect Mpox

- A patient presents with a typical clinical syndrome – pox-like rash or other typical feature.

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- Has appropriate epidemiologic exposure – contact withs someone else with Mpox or recent travel to Central or West Africa during time of outbreak.

*When suspected, do PCR testing for diagnosis.

*Avoid testing those without appropriate risk.

Diagnosis

- Should be diagnosed clinically first.
  - Therapy should not wait for definitive diagnosis.
- For definitive diagnosis: send Monkeypox virus PCR.
  - Swab lesion – 2 swabs per lesion – place entire swab in a sterile container and sent to lab.
  - Swab lesion vigorously. No need to un-roof lesion.
  - Swab at least two lesions/sites.
- Serology – if PCR testing is not available.
  - IgM positive about 5 days after rash onset, for 8 wks.
  - IgG positivity occurs around day 8 after rash onset.

Treatment

- Treatment is usually supportive in mild/moderate cases, but may consist of an antiviral medication, in severe or high-risk cases.
- PEP – MVA vaccine. Best if given within 4 days.
  - Vaccinia Immunoglobulin is also an option.
- Both treatment and vaccines are believed to be effective regardless of strain or clade.

Treatment

- Mild disease / low-risk patients – supportive care.
  - Send patient home and isolate until all lesions have new skin.
- Severe disease or HR pts – specific antiviral therapy or PEP.
  - Tecovirimat or Brincidofovir – most data is from animal models.
  - Tecovirimat is preferred 1st line – Inhibits orthopox protein.
    - Available for high-risk patients – start treatment early.
    - Available orally or via IV – and is well tolerated.
    - There is mounting data on human efficacy.
    - Usual adult dose is 600 mg BID for 14 days.
  - Brincidofovir 200 mg weekly x 2 wks – less data, liver toxicity.
  - Cidofovir – extremely toxic – renal failure. No data.
  - In patients with HIV, initiate ART ASAP.
  - Taper immunosuppressive meds if possible.

Indication to use Tecovirimat

- Severe immunocompromise (watch out for DIs).
- Pregnant women
- Children <18
- Patients with life threatening involvement or protracted disease.
- Mucosal lesions or ocular involvement.
- Lesions that cause severe pain.

Treatment in Advanced AIDS

- Don’t delay initiation of Mpox-specific therapy.
  - Don’t wait for diagnostic results, if strongly suspected.
- Tecovirimat is first line.
  - Resistance has been reported after prolonged therapy.
  - Consider dual therapy with Tecovirimat and Brincidofovir in very low CD4 patients who will need long-term therapy.
- Start ART immediately, if possible.

Mortality

- Significantly higher in clade 1 vs clade 2.
- Current clade 1 outbreak mortality rate is 4%, but 11% in young children (<5 yo).
- Prior clade 1 outbreaks had a 10% overall mortality rte.
- Clade 2 has had an overall mortality rate of (<0.1%), unless with advanced HIV.
  - Nigeria 2018 outbreak with clade 2 had 3.6% mortality

Prevention

- Smallpox vaccination – smallpox/monkeypox vaccine approved in US in 2019 – MVA – Modified Vaccinia Ankara vaccine. Overtaking previous live vaccine.
  - Attenuated vaccine, so safe in IC patients.
  - Excellent safety profile.
  - African study in 2005 looked at 2278 household contacts of monkeypox patients and found that prior smallpox vaccination had lower rates of infection (1.3%) vs unvax (7.5%).
  - History of past smallpox vaccination – efficacy 80%.
- 2 shots 4 weeks apart.

Infection Prevention

- Avoid contact with potentially infected animals.
- Avoid intimate or close contact with anyone who is sick with possible Monkeypox. Wash hands.
  - Avoid contact with their bedding, towels, etc.
  - Isolate infected patients. Use PPE when caring for them.
- Infection Control Practices for suspected cases: standard, contact, droplet and airborne.
  - Once fully crusted and new skin growing, isolation may be discontinued.
- Exposed should be monitored for 21 days for symptoms – duration of incubation period.

Any Questions?

Question 1

Mpox transmission commonly occurs through all of the following except:

A. Direct contact with skin lesions.
B. Respiratory droplets.
C. Sexual contact.
D. Maternal-fetal transmission.
E. Coming into contact with infected animals.

Answer: B

Question 2

Risk factors for more severe or protracted disease, include:

A. HIV infection with a CD4 of 450 and UD VL.
B. Pregnancy
C. Young adults between 25-40 years old.
D. Children under 5 years of age.
E. A and B
F. B and D.

Answer: F

Question 3

Which statement(s) is/are true about Mpox infection?

A. Patients are most infectious while they have rash.
B. Clade 2 is more common and more deadly than Clade 1.
C. Lymphadenopathy is rarely seen in Mpox, but is common in smallpox.
D. Patients usually have fever for at least 2 weeks.
E. A and C.
F. B and D.

Answer: E

Question 4

Which statements regarding antiviral therapy are true? Choose all correct answers.

A. All patients with diffuse rash should be treated with tecovirimat.
B. Patients with AIDS / CD4 <50 should be considered for dual therapy with tecovirimat and brincidofovir.
C. Cidofovir will likely become first line due to excellent safety profile.
D. All children <18 should be treated.
E. Should always wait for confirmed diagnosis prior to starting specific antiviral therapy.

Answers: B and D