Department of Pathology
College of Medicine

Introduction to Monkeypox

Roger A. Mitchell Jr. MD FCAP
Professor and Chairman
Department of Pathology
Howard University College of Medicine
Howard University Hospital


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MONKEYPOX
MGN

MONKEYPOX IN THE US

EPIDEMIOLOGY OF HUMAN MONKEYPOX VIRUS (MPXV)

- The first cases of human monkeypox were reported in Zaire in1970
- Endemic to the rural tropical rain forest villages of central and western Africa
- MPXV is one of the 4 orthopoxvirus species pathogenic for humans:
  - (1) variola major virus (VARV), the causative agent of smallpox, now eradicated,
  - (2) variola minor virus, and
  - (3) cowpox virus (CPXV).
- There is a range of animal poxviruses, several of which have zoonotic potential. Infections in humans have been described for vaccinia virus, cowpox virus, buffalopox virus, and sporadic cases of camelpox. Monkeypox infects a wide range of mammalian species, but its natural host reservoir remains unknown.
- The term is inappropriate because the largest animal reservoirs of the virus have been found in rodents, including squirrels and giant pouched rats, both of which are hunted for food.
- Primary monkeypox infection may be acquired via direct contact of the skin or mucosa with infected animals, whereas secondary transmission may occur via aerosol exposure like the usual route of exposure for smallpox.

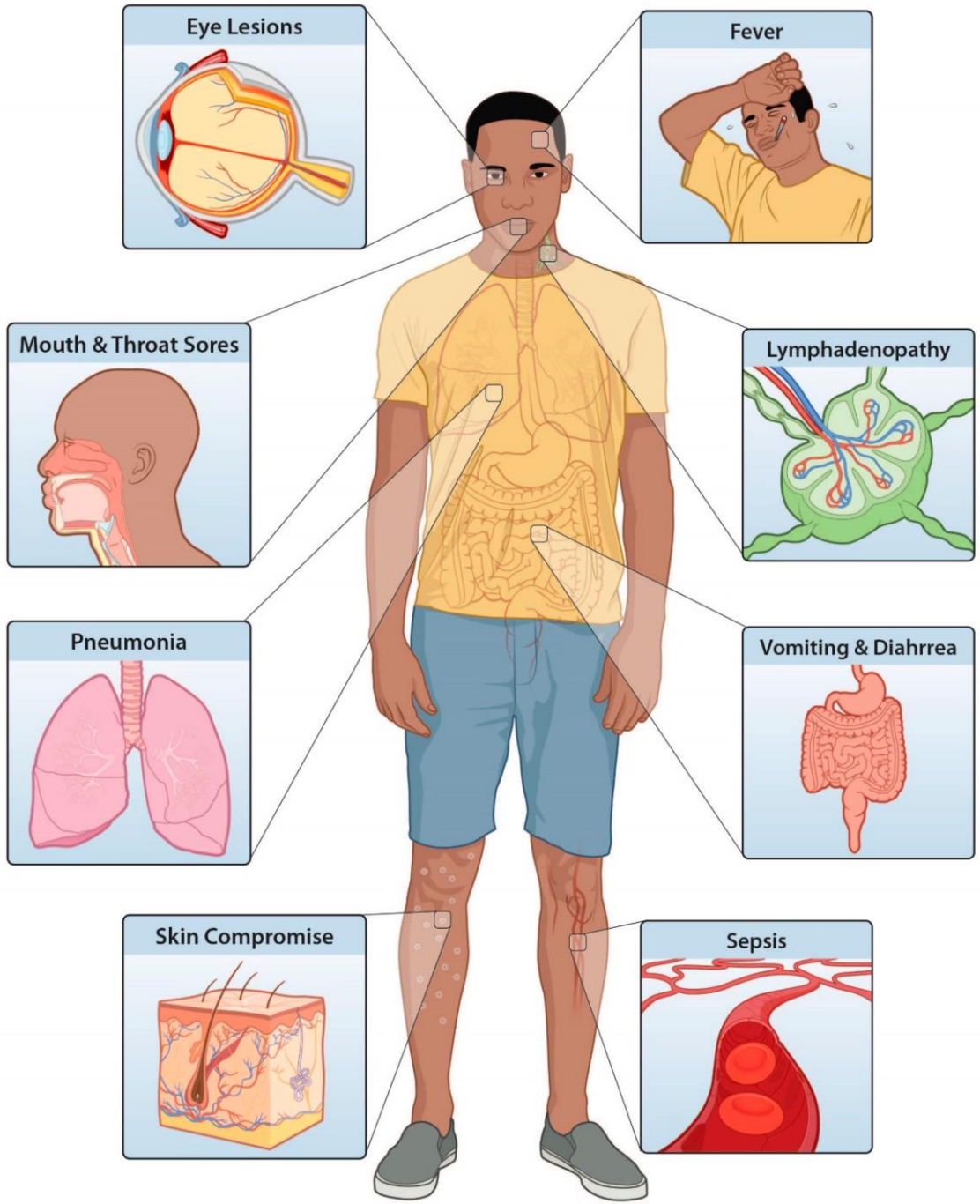
RARE AND SELF-LIMITING DISEASE


TUNISIA
MOROCCO
ALGERIA
LIBYA
EGYPT
WESTERN SAHARA
MAURITANIA
MALI
NIGER
CHAD
SUDAN
ERITREA
CAPE VERDE
SENEGAL
THE GAMBIA
BURKINA FASO
DJIBOUTI
GUINEA-BISSAU
GUINEA
BENIN
NIGERIA
SOMALIA
SIERRA LEONE
COTE D' IVOIRE
GHANA
CENTRAL AFRICAN REPUBLIC
SOUTH SUDAN
ETHIOPIA
LIBERIA
TOGO
CAMEROON
EQ. GUINEA
SÃO TOMÉ AND PRÍNCIPE
GABON
CONGO
UGANDA
KENYA
RWANDA
DR CONGO
SEYCHELLES
BURUNDI
TANZANIA
COMOROS
MAYOTTE
ANGOLA
MALAWI
ZAMBIA
MOZAMBIQUE
MADAGASCAR
ZIMBABWE
MAURITIUS
NAMIBIA
BOTSWANA
RÉUNION
SWAZILAND
LESOTHO
SOUTH AFRICA
Countries Reporting Monkeypox cases to WHO (1970–2019)
ST.HELENA

VACCINATION

- Various orthopoxvirus species share genetic and antigenic features, and an infection by any of these species may confer substantial protection against infection by the others.
- Vaccination with vaccinia virus protects against disease caused by VARV, MPXV, or CPXV.
- The immunologic mechanisms underlying cross-protection by immunization with vaccinia virus seem to be diverse, with neutralizing antibodies among the principal components

Indirect or Direct contact with live or dead animals is assumed to be the driver of human monkeypox infections in humans




A
B

CLINICAL SYMPTOMS

- 2-day prodrome prior to the onset of the rash, manifested by fever, malaise and severe lymphadenopathy.
- The rash begins with maculopapular lesions 2–5mm in diameter (starts usually on the face).
  - It spreads to become generalized in most cases.
- The typical skin lesion progresses through a papular, vesicular, pustular and crust stage over a 14- to 21-day period, before sloughing of the crust leaves a depigmented scar.
- A range of complications has been reported, such as secondary bacterial infections, respiratory distress, bronchopneumonia, encephalitis, corneal infection with ensuing loss of vision, gastrointestinal involvement, vomiting, and diarrhea with dehydration.
- Mortality is higher among children and young adults and the course is more severe in immunocompromised individuals.

a) early vesicle, 3mm diameter

b) small pustule, 2mm diameter

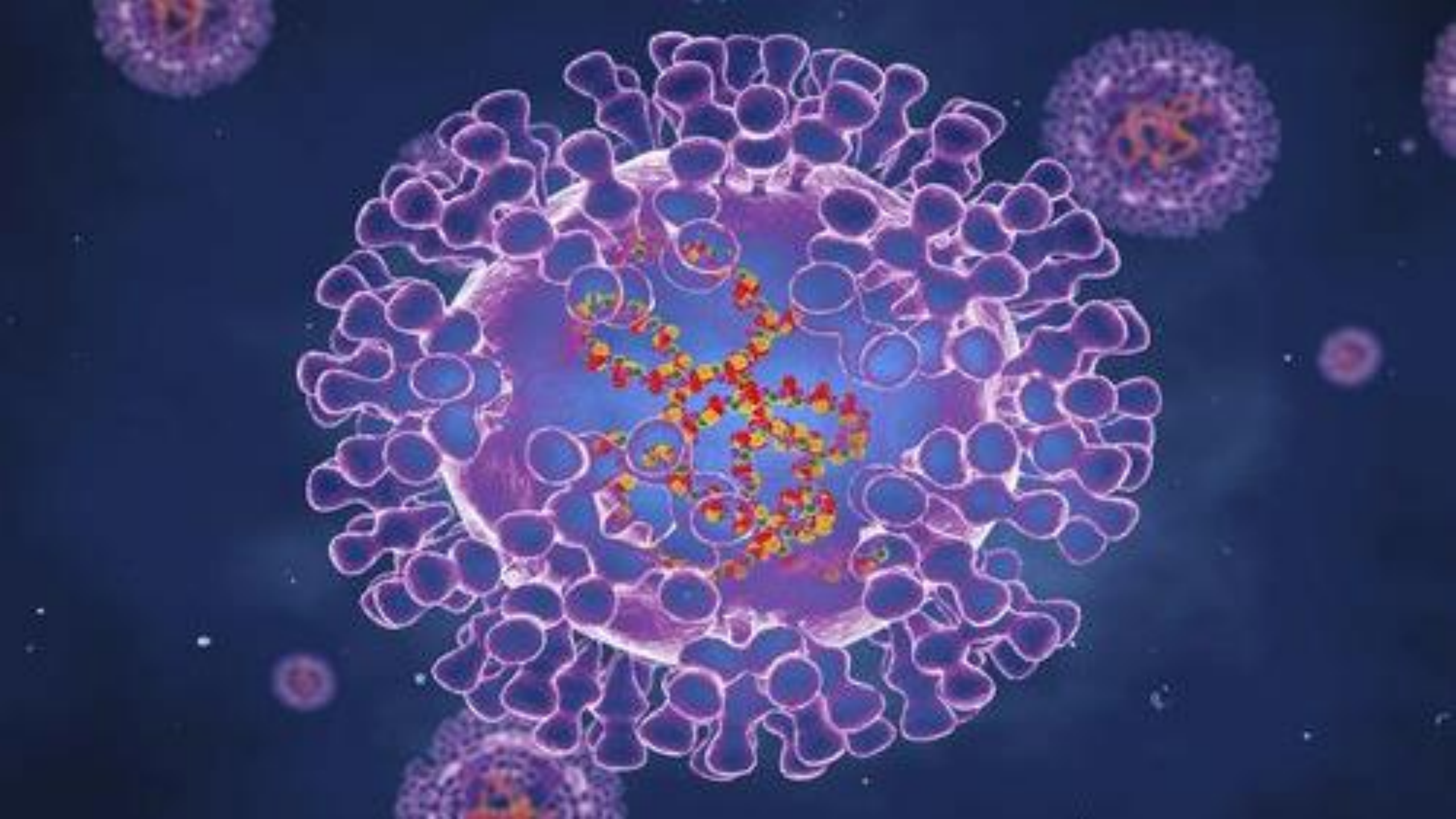
c) umbilicated pustule, 3-4mm diameter

d) ulcerated lesion, 5mm diameter

e) crusting of a mature lesion

f) partially removed scab

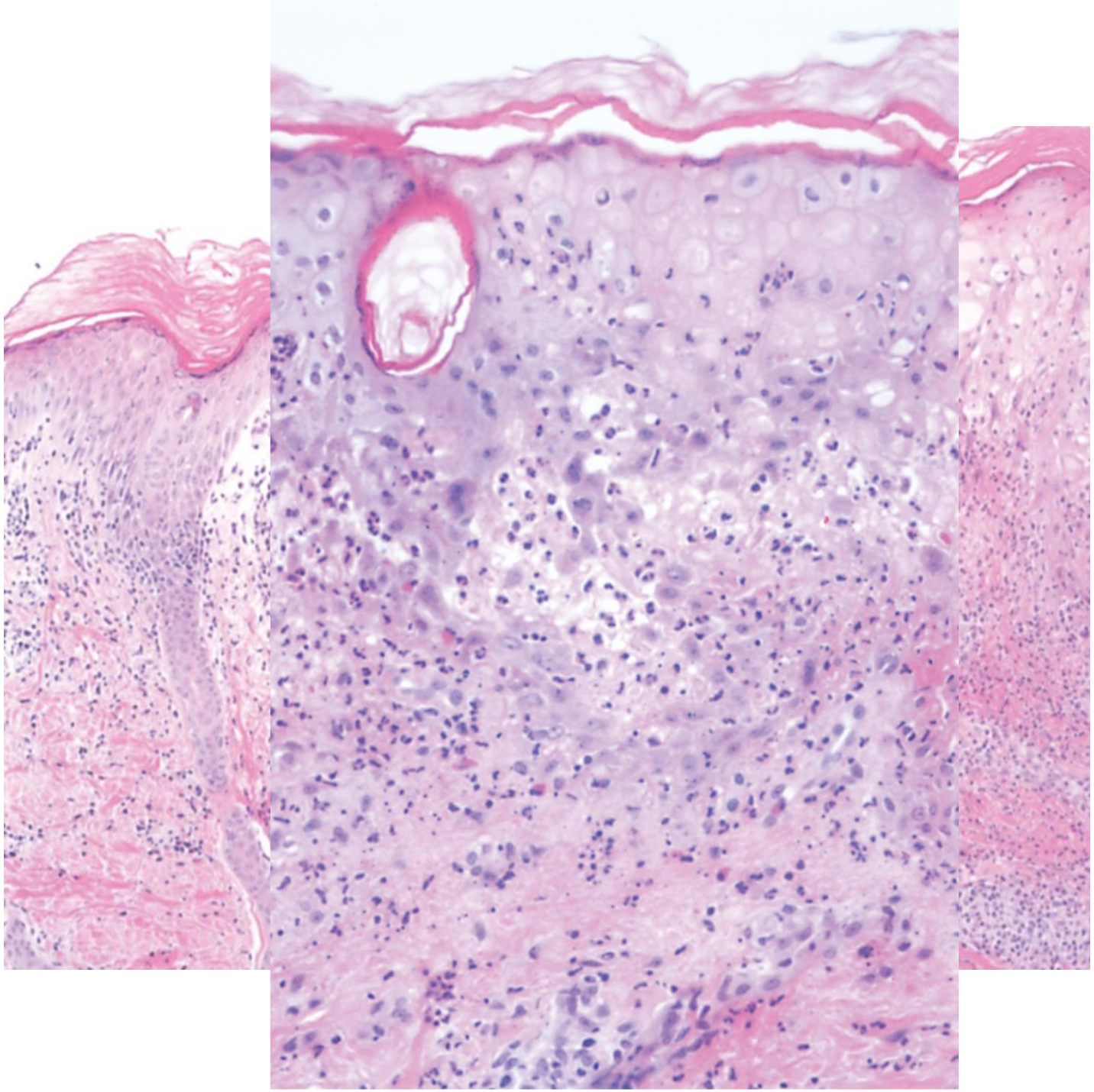
https://newshunt365.net/first-potential-human-to-human-transmission-of-monkeypox-detected-in-the-united-states/



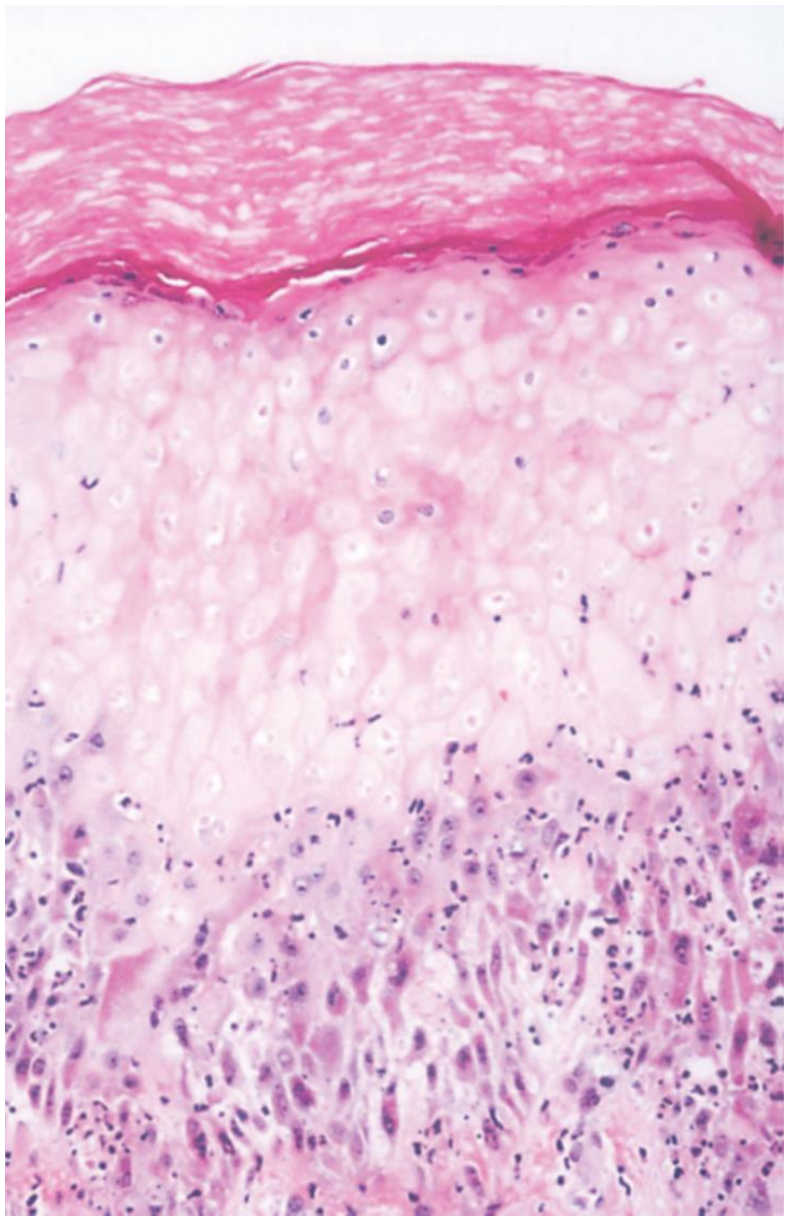
HISTOLOGY

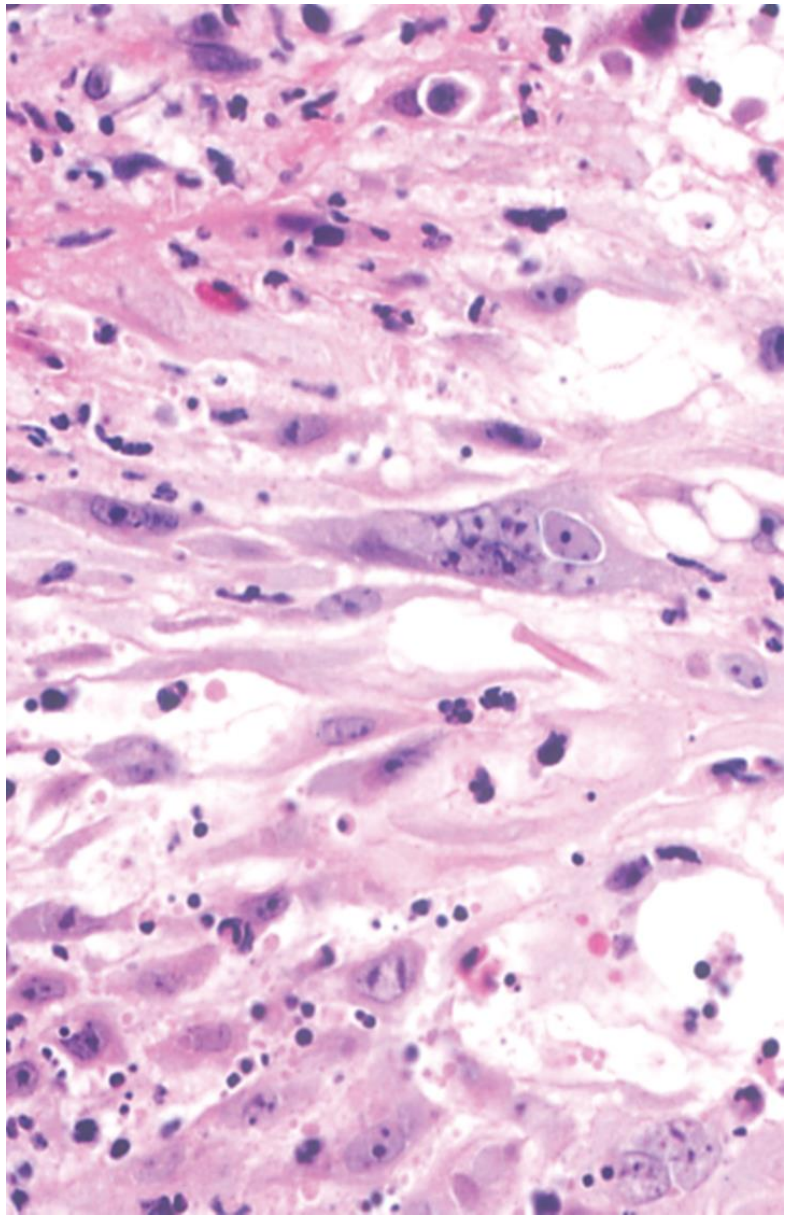
- The clinical progression of lesions is mirrored histologically with ballooning degeneration of basal keratinocytes and spongiosis of a mildly acanthotic epidermis progressing to full thickness necrosis of a markedly acanthotic epidermis containing few viable keratinocytes.
  - Like those of other viral exanthems, including those of variola, cowpox, varicella-zoster and herpes simplex virus (HSV)
- A lichenoid-mixed inflammatory cell infiltrate is present, which exhibits progressive exocytosis with the keratinocyte necrosis. Inflammation of the superficial and deep vascular plexes, eccrine units and follicles is also present.
- Viral cytopathic effect is manifest by multinucleated syncytial keratinocytes.
- Immunohistochemically, viral antigen is detected within keratinocytes of the lesional epidermis, follicular and eccrine epithelium and few dermal mononuclear cells. Electron microscopy reveals virions at various stages of assembly within the keratinocyte cytoplasm.

VESICULAR STAGE BULLA

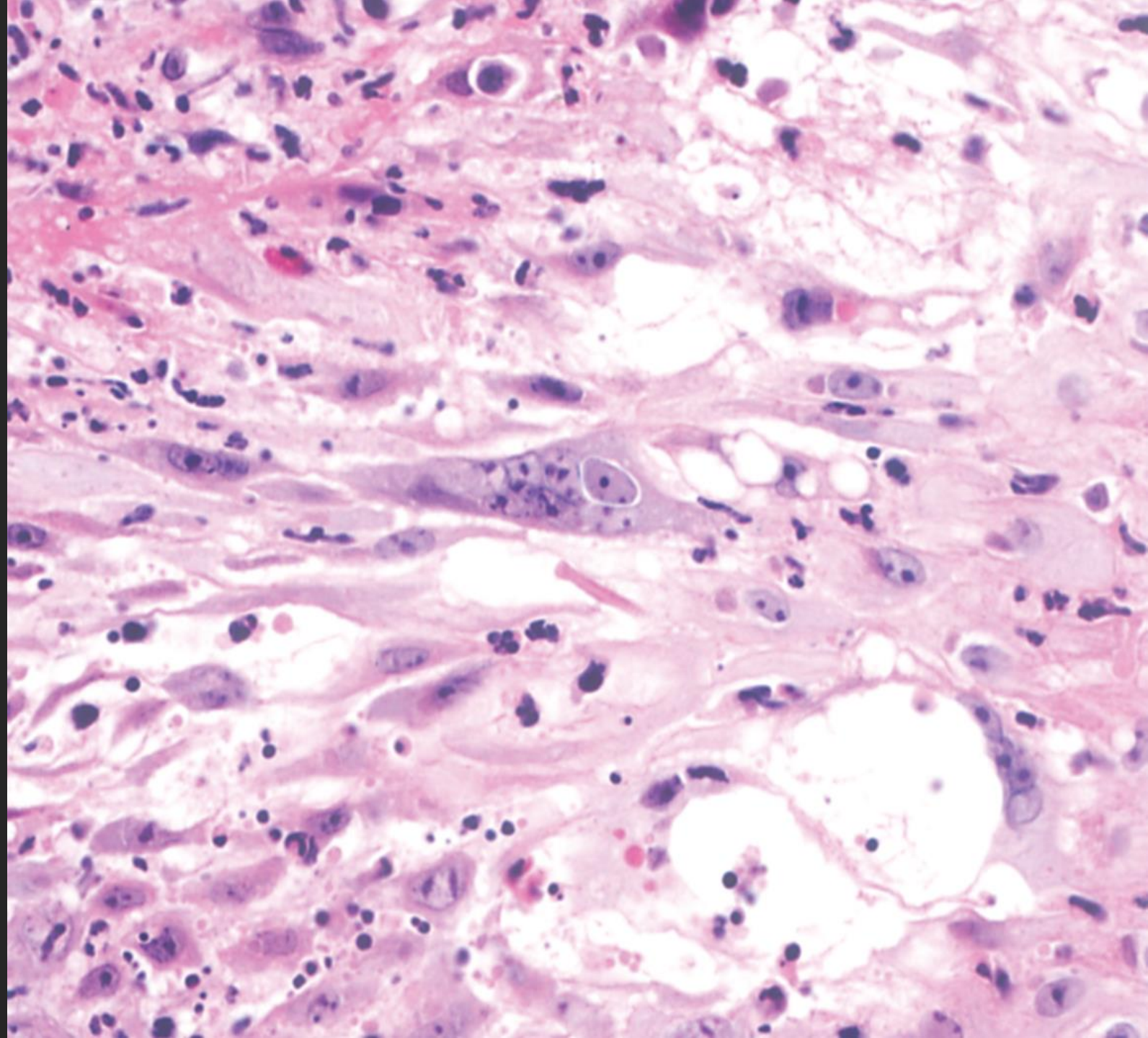


PUSTULAR STAGE BULLA

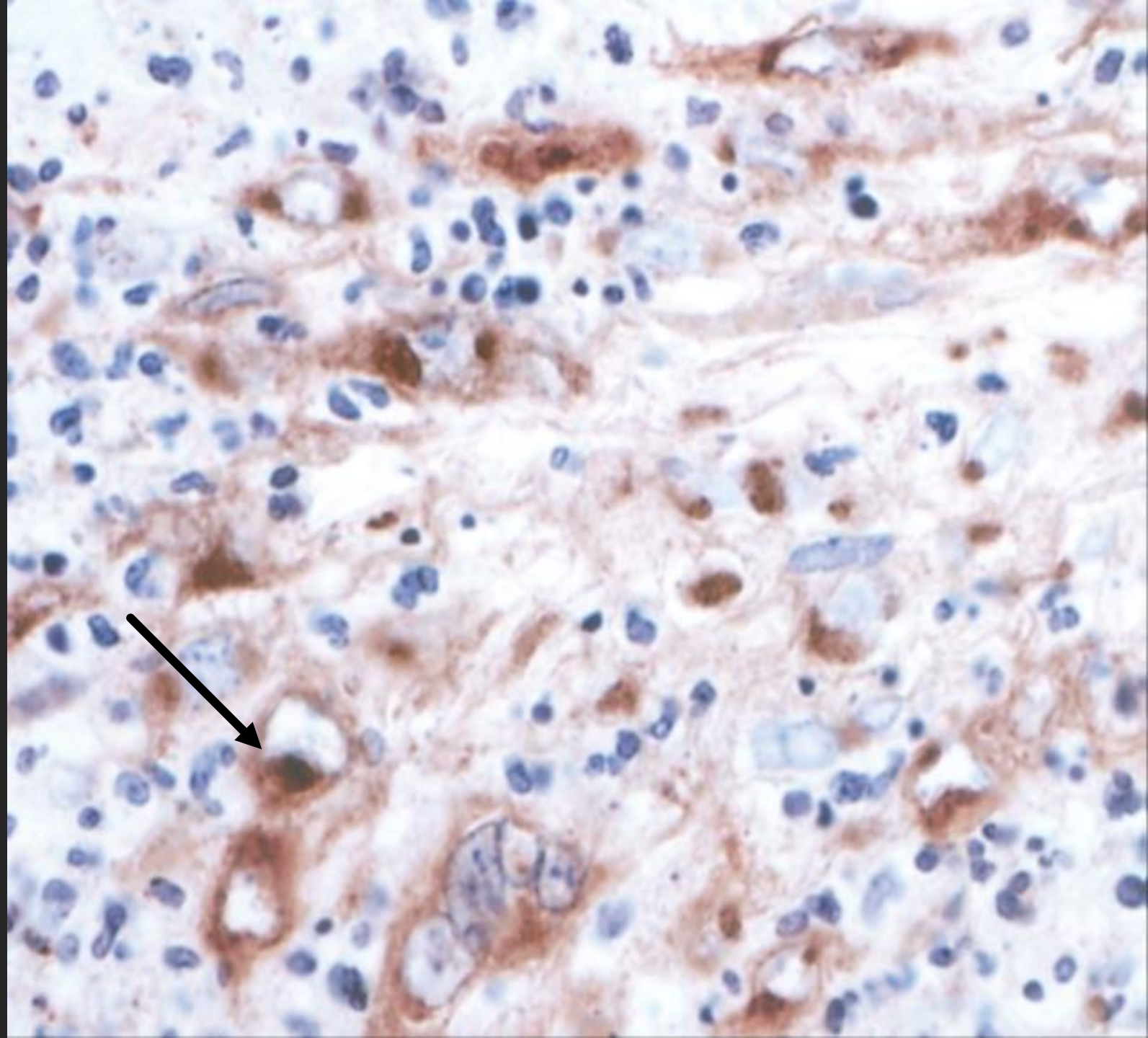


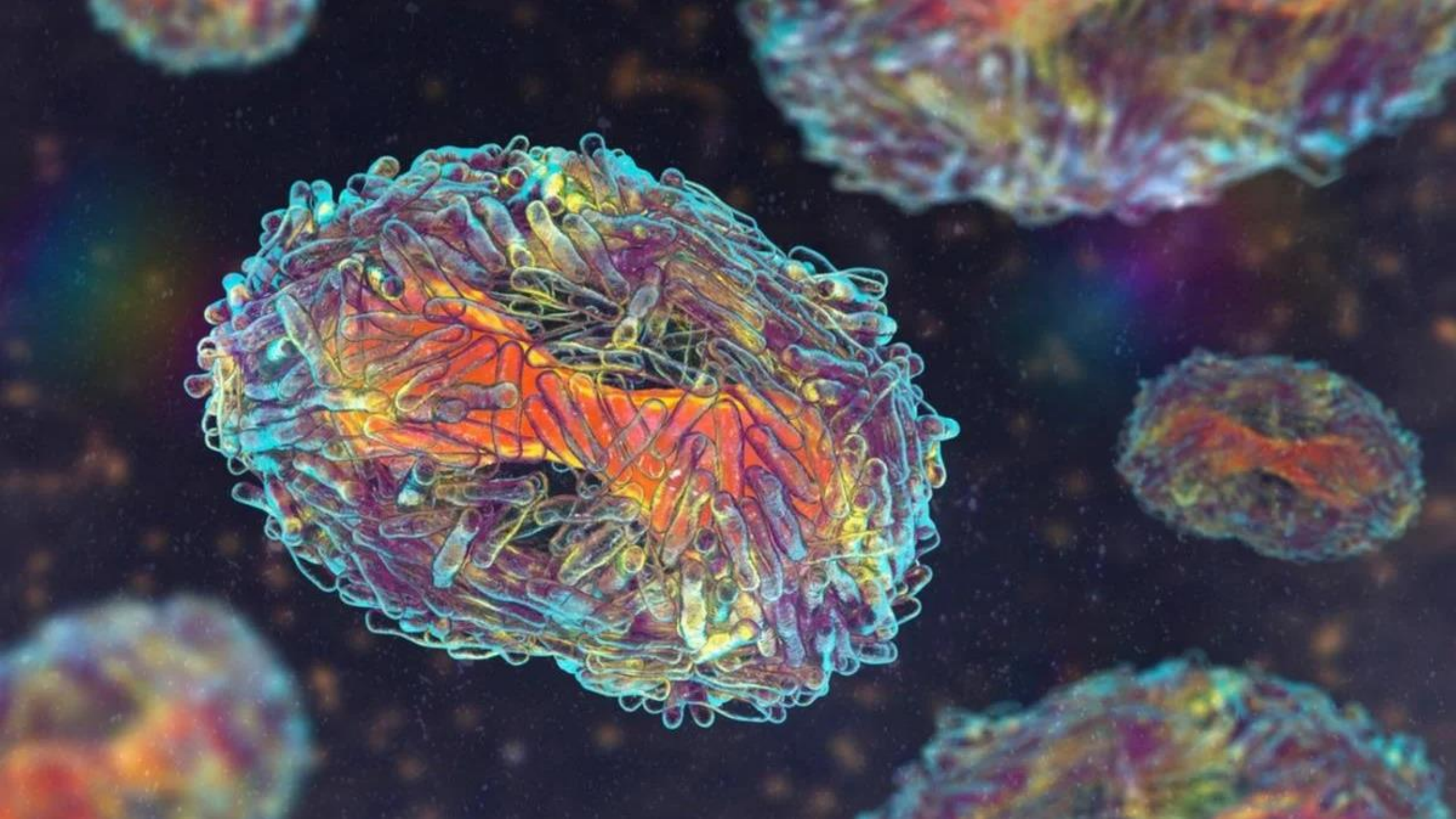


PUSTULAR STAGE BULLA

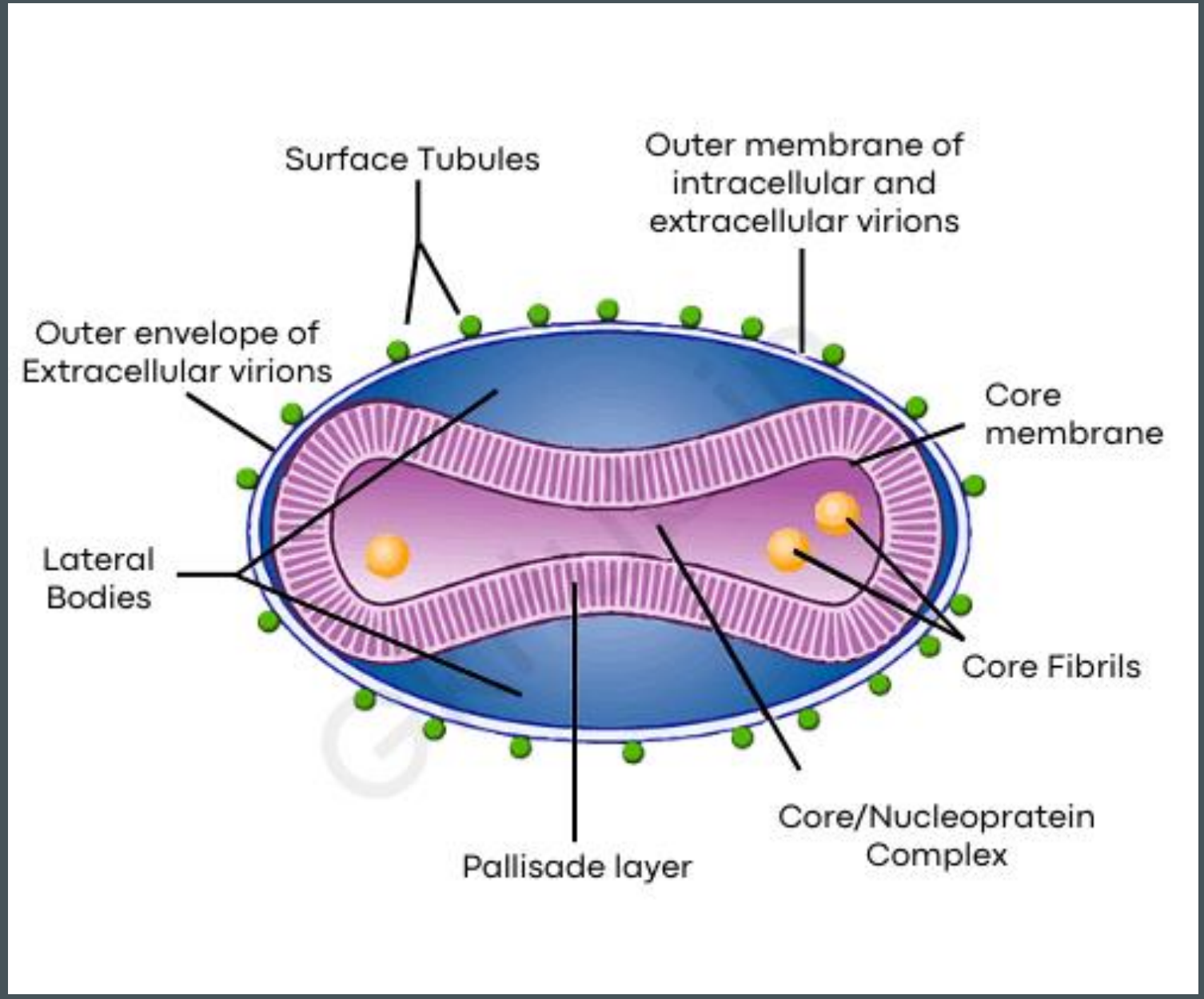


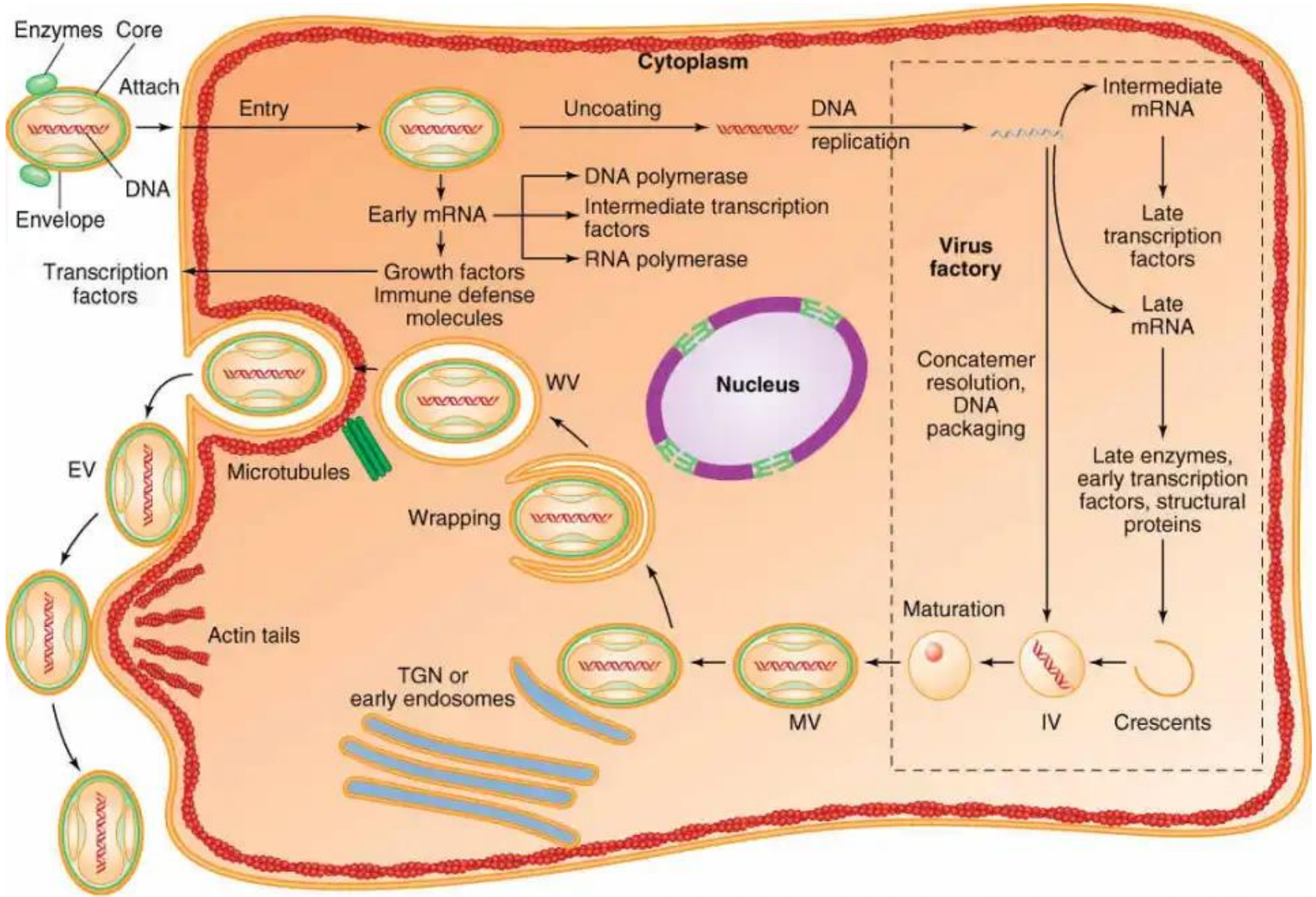
IHC WITH ANTI-VACCINIA ANTBODY





HUMAN MONKEYPOX VIRUS (MPXV) IS A DOUBLE-STRANDED DNA VIRUS OF THE ORTHOPOXVIRUS GENUS OF THE FAMILY POXVIRIDAE



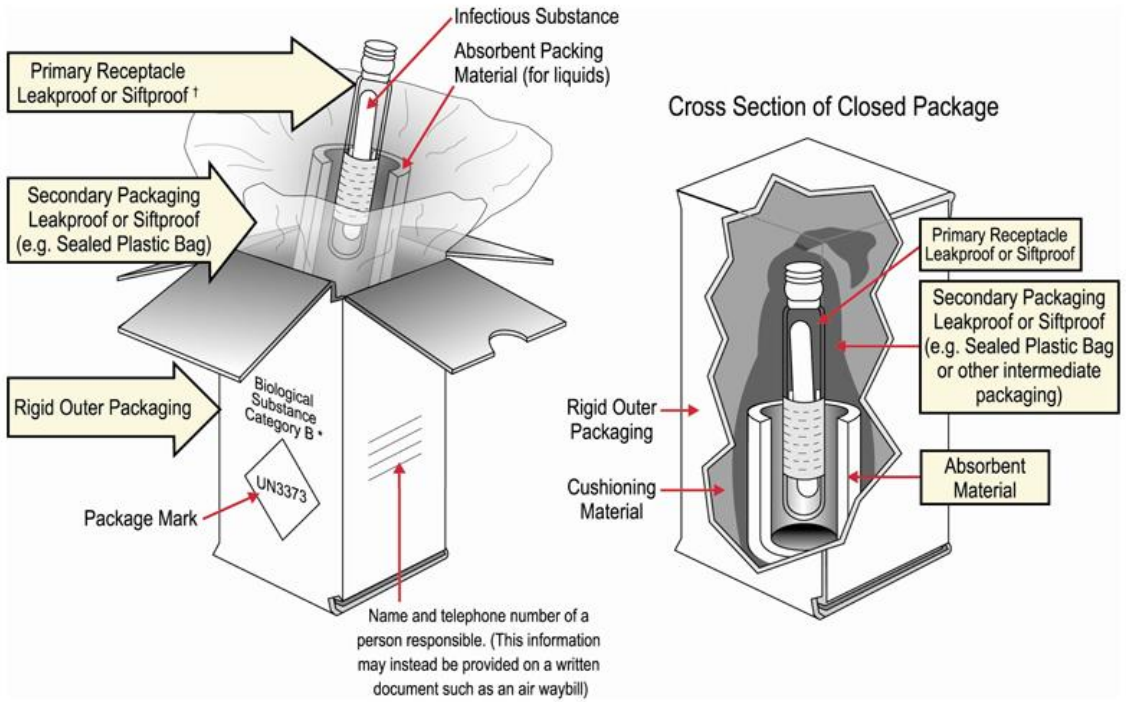


Information from Moss, B. *Poxviridae*. In *Fields Virology*, 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2013.

LABORATORY AND DIAGNOSTIC GUIDANCE

Specimen handling for suspected monkeypox samples

1. When you receive samples in the lab DO NOT OPEN. Please handle all suspected samples in Molecular room Biological Safety Cabinet
2. Gather following PPE and take the sample to Biological Safety Cabinet in Molecular (Panther) testing room.
    a. disposable gloves
    b. solid front gowns with cuffed sleeves
    c. face protection
3. Use absorbent pad spayed with freshly made 10% bleach (make daily) and use double bags for waste.
    a. Laboratory should receive two separate sterile dry polyester or Dacron swabs places in sterile container with NO LIQUID.
    b. Label each individual container with two unique patient identifiers.
    c. Specimens must be refrigerated or frozen at –20C or lower within 1 hour of specimen collection.



LABORATORY AND DIAGNOSTIC GUIDANCE

Specimen handling for suspected monkeypox samples

4. Submit specimens to DFS-PHL in an approved **Category A biohazard container containing a frozen cold pack** (if refrigerated) or on dry ice (if frozen).
5. Foe any reason if any samples need Centrifugation please follow following steps.
   a. must be performed using safety cups or sealed rotors.
   b. Rotors or safety cups should be opened in a BSC after centrifugation involving monkeypox specimens.
6. Follow these steps when disposing waste.
   a. Place all the items used in double red trash bag.
   b. Secure the bag and place in red biohazard trash container in Molecular room

LABORATORY AND DIAGNOSTIC GUIDANCE

Specimen handling for suspected monkeypox samples

7. Appropriate Documentation: Complete the following paperwork to accompany specimens from each patient. Place all paperwork on the outside of the box.
    a. A separate test requisition and 50.34 form must be filled out for each swab site. (this form is typically completed by the health care provider ordering the test) https://dfs.dc.gov/sites/default/files/dc/sites/dfs/publication/attachments/CDC_50-34.pdf
    b. DC DFS-PHL Test Requisition Form. Under BT Rule Out Other: Write in Monkeypox. https://dfs.dc.gov/sites/default/files/dc/sites/dfs/publication/attachments/DC_DFS-PHL_Test_Request_2022_1.pdf
    c. External Chain of Custody (COC) Form - Ensure this form can be seen from the outside. https://dfs.dc.gov/sites/default/files/dc/sites/dfs/publication/attachments/External_Chain_of_Custody_09032019.pdf

LABORATORY AND DIAGNOSTIC GUIDANCE

Specimen handling for suspected monkeypox samples

8. Courier Requests

Once specimens are ready for pick up and the appropriate documentation is completed, please submit a courier request:
https://forms.office.com/pages/responsepage.aspx?id=8Unkj5SLt0ZBmTnagtc9lcOHWVYmlPnkNKIOBwQopUMDRDSEU1VEhGTkEwVURRMzVSNDk2TVFESS4u

Following information will be requested.

a) Name of submitter
b) Submitter's email address.
c) Facility name.
d) Address of facility (pick-up address).
e) Date for courier request.
f) Type of courier request.
g) Additional comments and instructions.
h) Point of contact's name and phone number.
i) Number of specimens.

Turn-around time for CDC confirmation

Anticipated to be 24 – 48 hours from receipt at CDC; up to 5 business days

REFERENCES

- Bayer-Garner I. B. (2005). Monkeypox virus: histologic, immunohistochemical and electron-microscopic findings. Journal of cutaneous pathology, 32(1), 28–34. https://doi.org/10.1111/j.0303-6987.2005.00254.x
- Petersen, E., Kantele, A., Koopmans, M., Asogun, D., Yinka-Ogunleye, A., Ihekweazu, C., & Zumla, A. (2019). Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infectious disease clinics of North America, 33(4), 1027–1043. https://doi.org/10.1016/j.idc.2019.03.001

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Thank you!

roger.mitchell@howard.edu

202-806-6308