Monkeypox

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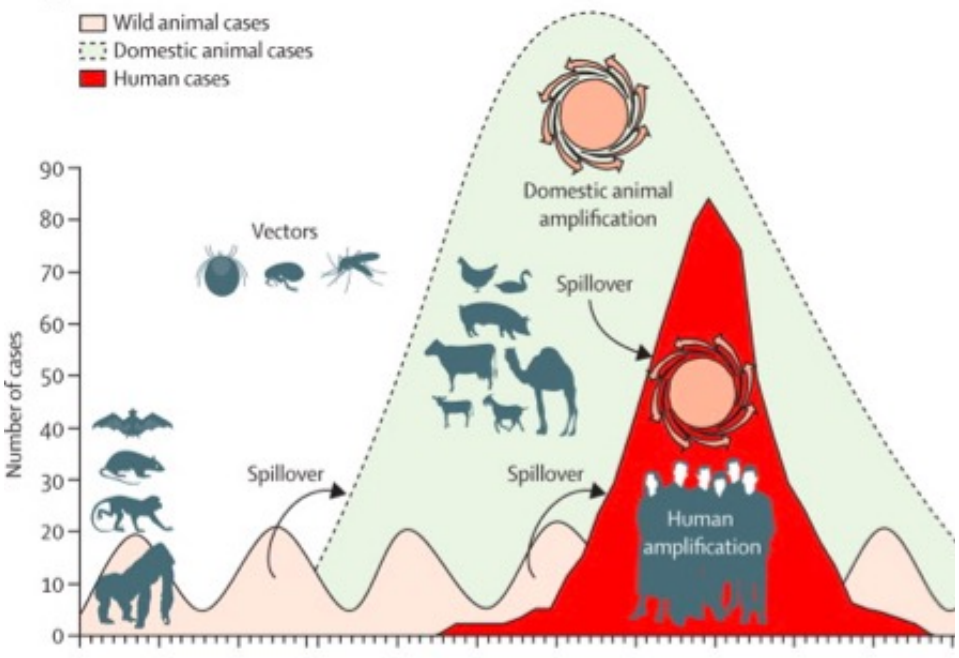
Disclaimers

- These slides represent partial knowledge of an evolving outbreak
- No conflicts of interest

Talk outline

- Discuss the biology of monkeypox
- Contextualize the current outbreak with history
- Review the clinical presentation of monkeypox
- Discuss practical diagnosis and isolation of suspected cases
- Familiarize clinicians with post-exposure prophylaxis and treatment options

Talking about outbreaks



Reservoir host = Usual animal host in which a pathogen circulates

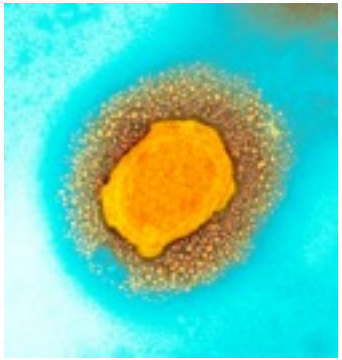
Zoonosis = a disease that infects humans from animal hosts

Emerging diseases = diseases that are increasing in human populations

Epidemic = an increase in cases of a disease in a population above expected

Pandemic = an epidemic in many places

Monkeypox virology



dsDNA virus
Genus: *Orthopoxvirus*
Family: *Poxviridae*

Famous relatives

Smallpox (variola virus)

- 30% mortality
- Led to understanding of variolation
- First disease for which there was a vaccine
- First disease eradicated

Cowpox

Vaccinia virus

Camelpox, ectromelia, horsepox, racoonpox, skunkpox, volepox…

Monkeypox thought of as a less deadly smallpox

Image from NLM, Kozlov et al 2022

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What's in a name

- Discovered in research colonies of monkeys in 1958
- Monkeys are **not** thought to be the reservoir hosts
- Rodent reservoir

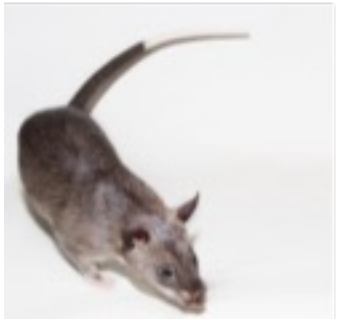

Table. Poxviruses That Infect Humans and Cause Disease.

Genus and Species (Disease)	Primary Reservoir	Geographic Region	Mode of Transmission	Protection Provided by Vaccinia Vaccination
Orthopoxvirus				
Cowpox	Rodents	Europe, Africa, central and northern Asia	Direct contact	Yes
Monkeypox	Rodents	Central and West Africa	Direct contact, respiratory droplets	Yes
Vaccinia	Unknown*		Direct contact	
Variola (smallpox)†	Humans	U.S., Russia	Direct contact, respiratory droplets	Yes

Images from Wikipedia, Frey and Belshe 2004

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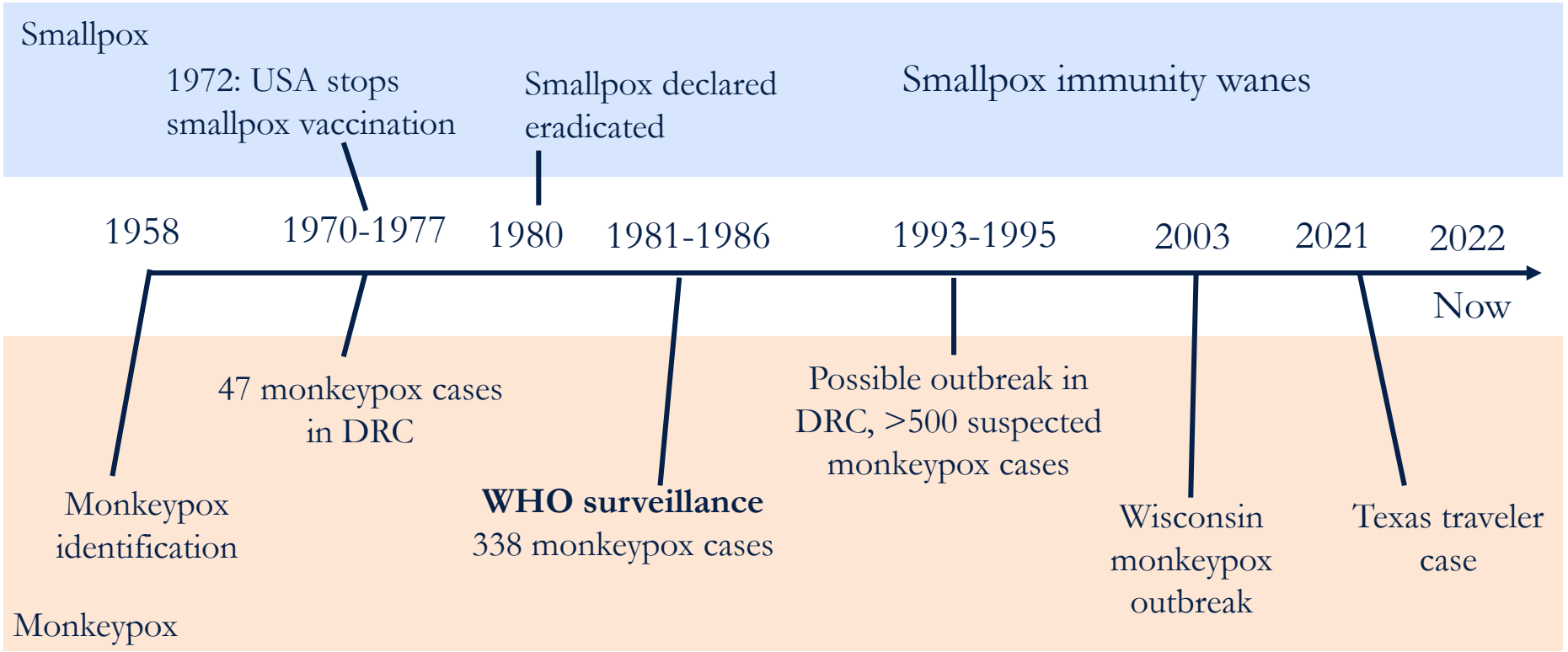
A partial history of monkeypox



Weinstein et al 2005

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The 2003 outbreak

- **Large outbreak in Wisconsin**
- 72 cases
  - No human-to-human transmission
  - No deaths
- All had contact with prairie dogs

- Prairie dogs are North American
- Animals had been kept next to Gambian pouched rats

The Detection of Monkeypox in Humans in the Western Hemisphere

Kurt D. Reed, M.D., John W. Melski, M.D., Mary Beth Graham, M.D., Russell L. Regnery, Ph.D., Mark J. Sotir, Ph.D., M.P.H., Mark V. Wegner, M.D., M.P.H., James J. Kazmierczak, D.V.M., M.S., Erik J. Stratman, M.D., Yu Li, Ph.D., Janet A. Fairley, M.D., Geoffrey R. Swain, M.D., M.P.H., Victoria A. Olson, Ph.D., et al.

Reed et al 2005; image from Wikipedia

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The current outbreak

- Worldwide: 1472 cases (6/10/22)
- USA: 49 confirmed cases (12 in California)
- Most have <u>not</u> been in patients who have traveled or had exotic animal contact

- Most but not all have been in patients who identify as men who have sex with men

CDC webinar; image from CDC website

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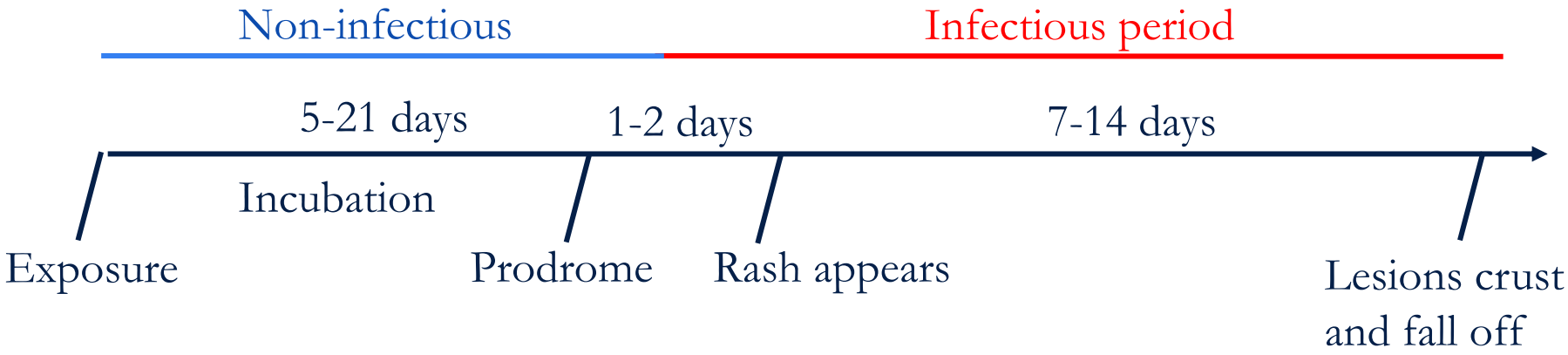
What's different this time?

	Prior outbreaks	2022
Case numbers	Limited	>1400 + growing rapidly
Transmission	Mostly zoonotic	Person-to-person
Geographic spread	Closely clustered	International
Presentation	Rash classically starts on face	Rash starts on genitals or anal area Sometimes no prodrome
Mortality	Estimates vary but ~10%	No deaths

Classic course of illness



Incubation = infected, but not infect*ious*, clinically well

Prodrome = 1-2 days, sx include fever, lymphadenopathy, sore throat, cough, malaise, headache

Infectious period = from prodrome to scabs falling off + skin healing

CDC website

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Timeline of rash

	Timing	Appearance	Mimics
Enanthem	~ 1 day?	First lesions in the mouth, tongue	HSV, GC/CG, syphilis
↓			
Maculopapular	2-4 days	Whole body rash, face +palms and soles	**2° Syphilis** Coxsackie (hand foot + mouth) Rocky mountain spotted fever
↓			
Vesicular	1-2 days	Raised + filled with fluid	
↓			
Pustular	5-7 days	Fluid becomes cloudy, umbilicated lesions	**HSV** (herpes) **VZV** (chickenpox)
↓			
Scabs	7-14 days		

CDC website; Images from Uptodate + Wikipedia

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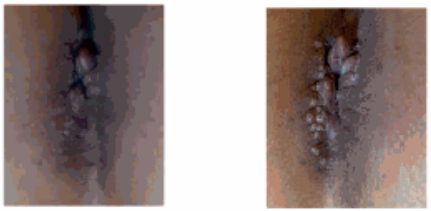
More about the rash

A. Genital area with rash, crusted monkey-pox and hand with pustule

B. Hand

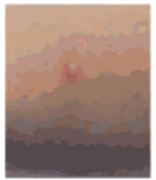
C. Shoulder area

A. Anal lesions



B. Genital lesions

C. Skin lesions



Hammerschlag et al 2022; Antinori et al 2022

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CDC case definitions

Epidemiologic criteria (within 21d)

1. Contact with a known or probable case
2. Travel to a country with confirmed cases of monkeypox
3. Contact with an African endemic animal, or a product derived from an animal
4. Patients who identify as MSM, as a group experiencing high rates of monkeypox

Exclusion criteria

1. Alternative diagnosis
2. No rash
3. High quality specimens are negative for *Orthopoxvirus* or Monkeypox virus

Suspect case = Rash + 1 epidemiologic criteria + clinical suspicion

Probable case:

1. Orthopoxvirus positive by PCR, IgM antibody, or EM or IHC, *and*
2. No other orthopoxvirus exposure (such as vaccinia virus in ACAM2000)

Confirmed case = Monkeypox virus detected by PCR, culture or mNGS

CDC website

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Transmission

	What it is	Examples
★ **Zoonotic**	Animal-to-human	Rabies, hantavirus
★ **Touch/Contact**	Touching lesions	Herpes, syphilis
★ **Droplet**	Requires big droplets (close face to face)	Flu
? **Airborne**	Tiny particles that stay suspended in air	TB

Monkeypox is thought currently to spread via zoonosis, contact with lesions or close face to face contact

CDC website

Monkeypox isolation precautions

- **Contact, airborne, droplet, and standard precautions**
- HCW should wear N95, eye protection, gown, and gloves
- Patient should be in an airborne infection isolation room (AIIR) if available
- If no AIIR, place patient in private room with door closed
- Patient should wear a mask

How to diagnose a patient; part 1

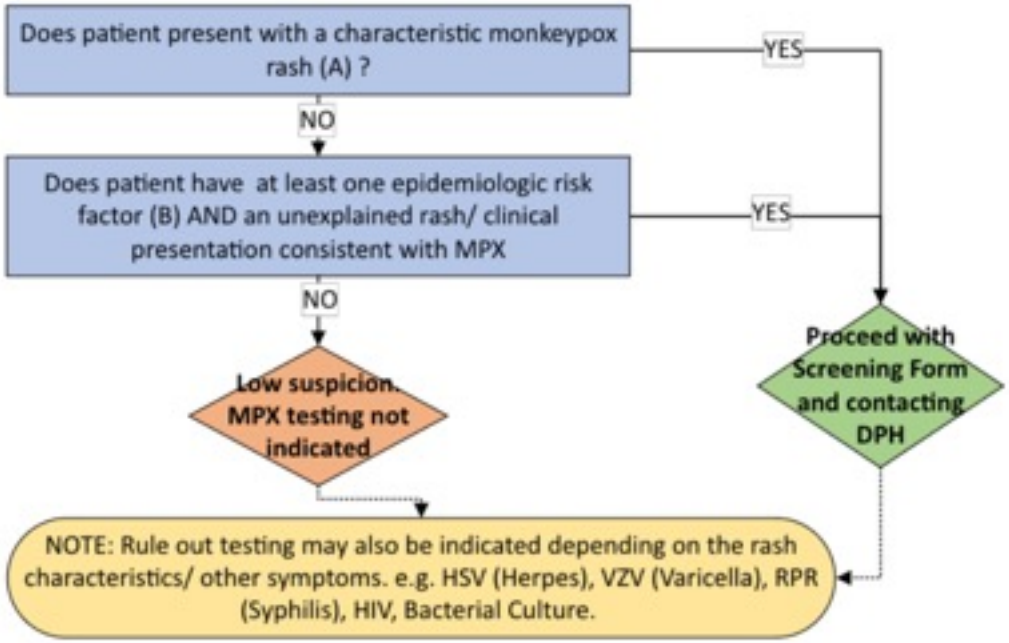
Step 0: Place on isolation

Step 1: Initial screening

Step 2: Gather information (Worksheet)

Step 3: Call Communicable Disease Control Unit (CDCU) on 415-554-2830

- **Step 3A:** call Micro to alert them



Debbie Yokoe; Stephanie Cohen; CDCU handout

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How to diagnose a patient; part 2

Step 4: Collect samples
- Collect 2 swabs from at least 3 lesions
- Unroof vesicles if possible
- Store at 4C if shipping w/in 24-48 hrs; -80C if longer

Step 5: Counsel the patient on isolation
- Warn about autoinoculation

Step 6: Disclose results

Stephanie Cohen; image from VWR

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Post-exposure prophylaxis

Who is this for?

Exposed but asymptomatic

- Close contacts of cases
- Health care workers

What is it

Monkeypox vaccine =
smallpox vaccine =
vaccinia virus =
a less virulent poxvirus

Vaccines

- ACAM200 = live, replication **competent** vaccinia virus
  - Risk of progressive vaccinia infection in immunocompromised patients
  - Risk of myopericarditis (5.7/1,000)
  - Not currently recommended

- JYNNEOS = live replication **incompetent** vaccinia virus
  - Theoretically no risk of progressive infection
  - Unknown risk of myopericarditis

PEP only available from CDC/DPH

CDC website; CDC MMWR 2009; CDC MMWR 2022

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Which patients to treat?

- Most cases of monkeypox will have mild, self limited disease

- Consider antivirals in the following cases:
  - Severe disease
    - Confluent lesions, encephalitis, hospitalized
  - Immunocompromised
  - Pediatric
  - Pregnant or breastfeeding
  - Complications (superinfection)
  - Monkeypox lesions **near mouth, eyes, or genitals**

Treatment

	What is it?	Evidence	Availability
Cidofovir	Antiviral Approved for CMV retinitis	In vitro, animal data Human data on other poxviruses	Available (in pharmacy)
Brincidofovir	Less nephrotoxic cidofovir	In vitro, animal data Human data for CMV	Not available
Tecovirimat ST-246	Antiviral	Used against monkeypox in animal model	Through DPH/CDC
Vaccinia immune globulin	Human antibodies against vaccinia	Used in cases of disseminated vaccinia	Through DPH/CDC

Merchlinksky et al 2009; Marty et al 2019; CDC website

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A word on stigma

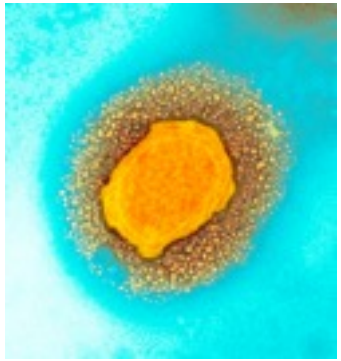
San Francisco reports major rise in anti-Asian hate crimes

Monkeypox: UNAIDS 'concerned' about stigmatizing language against LGTBI people

- Outbreaks can be associated with stigma and violence towards vulnerable groups

NBC News, UNAIDS

Conclusions



- Fast evolving situation
- Low case count at this time
- Remember syphilis, VZV, HSV are much more likely
- Reach out early to DPH/CDC to guide management
- Combat stigma and misinformation

Who to call

Infectious Disease

Infection Control

California SF DPH: 415-554-2830

CDC: 770-488-7100

Questions?

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