Monkeypox

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Monkeypox

- A rare disease that is caused by infection with monkeypox virus, it belongs to the Orthopoxvirus genus in the family Poxviridae.
- The Orthopoxvirus genus includes : variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), cowpox virus monkeypox virus





- Monkeypox was first discovered in 1958 when two outbreaks of a pox-like disease occurred in colonies of monkeys kept for research.
- The first human case of monkeypox was recorded in 1970 in the Democratic Republic of the Congo (DRC).

Since then, monkeypox has been reported in people in several other central and western African countries: Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Republic of the Congo, and Sierra Leone. The majority of infections are in Democratic Republic of the Congo.



Monkeypox cases in people have occurred outside of Africa linked to international travel or imported animals.



Figure 1. Geographical distribution of confirmed cases of MPX in EU/EEA countries, as of 25 May 2022



1 Geographical distribution of confirmed cases of MPX in EU/EEA countries, as of 25 May 2022

Figure 1. Geographical distribution of confirmed and suspected cases of monkeypox in non-endemic countries between 13 to 26 May 2022, 5 PM CEST.



Most monkeypox cases in the current outbreak are in men aged 20–50 years

Table 1. Cases of monkeypox in nonendemic countries to WHO between 13 May to 26 May 2022, 5 PM CEST

| Region | Country | Confirmed | Suspected under investigation |
|--------|---|-----------|----------------------------------|
| РАНО | Argentina | | 1 |
| | Canada | 26 | 25 - 35 |
| | French Guiana | | 2 |
| | United States of America | 10 | |
| EMRO | United Arab Emirates | 1 | |
| | Sudan | | 1 |
| EURO | Austria | 1 | |
| | Belgium | 3 | 3 |
| | Czechia | 2 | 1 |
| | Denmark | 2 | |
| | Finland | 1 | |
| | France | 7 | |
| | Germany | 5 | |
| | Israel | 1 | |
| | Italy | 4 | |
| | Netherlands | 12 | >20 |
| | Portugal | 49 | |
| | Slovenia | 2 | |
| | Spain | 20 | 64 |
| | Sweden | 2 | |
| | Switzerland | 1 | - |
| | United Kingdom of Great Britain and Northern Ireland | 106 | |
| WPRO | Australia | 2 | |
| TOTAL | 23 countries | 257 | 117-127 |



- The World Health Organization has received reports of 257 confirmed monkeypox cases and about 120 suspected cases in 23 nations where the virus is not endemic as of Thursday.
- In the United States, the Centers for Disease Control and Prevention has reported 12 cases in eight states as of Friday afternoon.

Table 2. Cases of monkeypox in endemic countries

| Country | Time period | Cumulative cases | Cumulative deaths |
|-------------------------------------|---------------------------------|-------------------------|--------------------------|
| Cameroon | 15 December 2021 to 1 May 2022 | 25 | 9 |
| Central African Republic | 4 March to 17 May 2022 | 8 | 2 |
| Democratic Republic of the Congo | 1 January to 8 May 2022 | 1284 | 58 |
| Nigeria | 1 January 2022 to 30 April 2022 | 46 | 0 |
| Republic of the Congo | 21 May 2022 to 23 May 2022 | 2 | 0 |

Monkeypox: Cumulative confirmed cases, by date of confirmation



Cases are shown by the date on which they were confirmed by a test.







- The first sequencing of the virus shows that the strain is not different from the strains we can find in endemic countries and (this outbreak) is probably due more to a change in human behaviour.
- "Among the 21 cases reported in 2022 so far in Nigeria , there has been NO evidence of any new or unusual transmission of the virus, nor changes in its clinical manifestation documented (including symptoms, profile and virulence)," NCDC said in a statement late on Sunday.

/ ۸ خرداد ۱۴۰۱ - ۱۵:۵۰ /

حیدری، معاون بهداشت وزارت بهداشت عنوان کرد

۹ مورد مشکوک آبله میمونی در ایران

هیچ مورد ثابت شده آبله میمونی در کشور نداریم

معاون بهداشت وزارت بهداشت گفت: ۹ مورد مشکوک آبله میمونی داشتیم که ۵ تا ۶ مورد منفی قطعی شدند و برای بقیه هم منتظر پاسخ آزمایش هستیم. الان هیچ مورد ثابت شده آبله میمونی در کشور نداریم.





رئیس اداره مراقبت بیماری های واگیر وزارت بهداشت، از شناسایی ۶ بیمار مشکوک به آبله میمون در کشور خبر داد.

Reservoir host



- Still unknown although African rodents are suspected to play a part in transmission.
- The virus has only been isolated) twice from an animal in nature. In the first instance (1985), the virus was recovered from an apparently ill African rodent (rope squirrel) in Democratic Republic of Congo. In the second (2012), from a dead infant mangabey found in the Tai National Park, Cote d'Ivoire.



Transmission

- Direct contact with the virus from an animal, human, or materials contaminated with the virus.
- The virus enters the body through broken skin (even if not visible), respiratory tract, or the mucous membranes (eyes, nose, or mouth).
- Animal-to-human transmission may occur by bite or scratch, bush meat preparation, direct contact with body fluids or lesion material, or indirect contact with lesion material, such as through contaminated bedding.



- Human-to-human transmission is thought to occur primarily through large respiratory droplets, so prolonged face-to-face contact is required.
- Other human-to-human methods of transmission include direct contact with body fluids or lesion material, and indirect contact with lesion material, such as through contaminated clothing or linens.

Incubation period

► Usually 7–14 days but can range from 5–21 days.

- ► A person is **not contagious** during this period.
- ► A person does not have symptoms and may feel fine.

Signs and Symptoms

- In humans, the symptoms of monkeypox are similar to but milder than the symptoms of smallpox.
- Monkeypox begins with fever, headache, muscle aches, and exhaustion. A person may sometimes be contagious during this period.
- The main difference between symptoms of smallpox and monkeypox is that monkeypox causes lymphadenopathy while smallpox does not. Lymph nodes may swell in submandibular & cervical, axillary, or inguinal and occur on both sides of the body or just one.

The illness begins with:

- Fever
- ► Headache
- Muscle aches
- ▶ Backache
- Swollen lymph nodes
- ► Chills
- Exhaustion



- Within 1 to 3 days (sometimes longer) after the appearance of fever, the patient develops a rash, often beginning on the face.
- Lesions progress through the following stages before falling off:

Macules Papules Vesicles Pustules Scabs





- Vesicles or pustules that are deep-seated, firm or hard, and wellcircumscribed; the lesions may umbilicate or become confluent and progress over time to scabs.
- A person is contagious from the onset of the enanthem through the scab stage.
- Pitted scars and/or areas of lighter or darker skin may remain after scabs have fallen off.
- Once all scabs have fallen off a person is no longer contagious.

Enanthem Through the Scab Stage

| Stage | Stage Duration | Characteristics |
|----------|-------------------|--|
| Enanthem | | •The first lesions to develop are on the tongue and in the mouth. |
| Macules | 1–2 days | Following the enanthem, a macular rash appears on the skin, starting on the face and spreading to the arms and legs and then to the hands and feet, including the palms and soles. The rash typically spreads to all parts of the body within 24 hours becoming most concentrated on the face, arms, and legs (centrifugal distribution). |
| Papules | 1-2 days | •By the third day of rash, lesions have progressed from macular (flat) to papular (raised). |
| Vesicles | 1-2 days | •By the fourth to fifth day, lesions have become vesicular (raised and filled with clear fluid). |
| Pustules | 5–7 days | By the sixth to seventh day, lesions have become pustular (filled with opaque fluid) – sharply raised, usually round, and firm to the touch (deep seated). Lesions will develop a depression in the center (umbilication). The pustules will remain for approximately 5 to 7 days before beginning to crust. |
| Scabs | 7-14 days | By the end of the second week, pustules have crusted and scabbed over. Scabs will remain for about a week before beginning to fall off. |

Key Characteristics for Identifying Monkeypox

- Lesions are well circumscribed, deep seated, and often develop umbilication (resembles a dot on the top of the lesion)
- Lesions are relatively the 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
- Lymphadenopathy common
- Disseminated rash is centrifugal (more lesions on extremities, face)
- Lesions on palms, soles
- Lesions are often described as painful until the healing phase when they become itchy (crusts)











- West African monkeypox is associated with milder disease, fewer deaths, and limited human-to-human transmission.
- Human infections with the Central African monkeypox virus clade are typically more severe compared to those with the West African virus clade and have a higher mortality.
- Preliminary data confirm that the genomes in this outbreak belong to the West African clade of monkeypox virus.

Case Definitions For Use: Monkeypox 2022

Person Under Investigation

are individuals who are reported as suspicious but have not been tested in an LRN laboratory.

Possible Case

Meets one of the epidemiologic criteria **AND** has fever or new rash **AND** at least one other sign or symptom with **Onset** 21 days after last exposure meeting epidemiologic criteria



Probable Case

Meets one of the epidemiologic criteria **AND** has **new rash** with or without fever **AND** at least one other sign or symptom with onset 21 days after last exposure meeting epidemiologic criteria **AND**

Demonstration of detectable levels of anti-orthopoxvirus IgM antibody during the period of 4 to 56 days after rash onset.



Confirmed Orthopoxvirus Case

Meets possible case definition **AND** Demonstration of orthopoxvirus DNA by polymerase chain reaction testing of a clinical specimen **OR** demonstration of presence of orthopoxvirus using immunohistochemical or electron microscopy testing methods



Confirmed Monkeypox Case

Meets possible case definition **AND**

Demonstration of 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 سروری، رئیس انستیتو پاستور ایران خبر داد

تامین کیتهای غربالگری آبله میمونی در انستیتو پاستور

توزیع کیتهای اولیه در آزمایشگاههای منتخب

رئیس انستیتو پاستور ایران از تامین کیتهای غربالگری آبله میمونی خبر داد و گفت: دانشگاههای علوم پزشکی منتخب در صورت تشخیص موارد مشکوک در آزمایشات غربالگری، نمونهها را برای بررسی تکمیلی به انستیتو پاستور ارسال خواهند کرد.

Exclusion Criteria

A case may be **excluded** as a possible, probable, or confirmed monkeypox case if:

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



- The rash associated with monkeypox can be confused with other diseases that are more commonly encountered in clinical practice (e.g., secondary syphilis, herpes, chancroid, and varicella zoster).
- Historically, sporadic reports of patients co-infected with monkeypox virus and other infectious agents (e.g., varicella zoster, syphilis).
- A high index of suspicion for monkeypox is warranted when evaluating people with a characteristic rash, particularly for men who report sexual contact with other men and who present with lesions in the genital/perianal area or for travel history in the month before illness onset or contact with a suspected or confirmed case of monkeypox.

Interim Clinical Guidance for the Treatment of Monkeypox

- Many individuals infected with monkeypox virus have a <u>mild, self-</u> <u>limiting disease course</u> in the absence of specific therapy.
- However, the prognosis for monkeypox depends on multiple factors such as previous vaccination status, initial health status, concurrent illnesses, and comorbidities among others.

Persons with severe disease requiring hospitalization

▶ Persons with immunocompromise (e.g., human immunodeficiency virus/acquired immune deficiency syndrome infection, leukemia, lymphoma, generalized malignancy, solid organ transplantation, therapy with alkylating agents, antimetabolites, radiation, tumor necrosis factor inhibitors, high-dose corticosteroids, being a recipient with hematopoietic stem cell transplant <24 months post-transplant or ≥24 months but with graft-versus-host disease or disease relapse, or having autoimmune disease with immunodeficiency as a clinical component)</p>

Persons with severe disease requiring hospitalization

- Pediatric populations, particularly patients younger than 8 years of age
- Pregnant or breastfeeding women
- Persons with one or more complications (e.g., secondary bacterial skin infection; gastroenteritis with severe nausea/vomiting, diarrhea, or dehydration; bronchopneumonia; concurrent disease or other comorbidities)
- Persons with aberrant infections that include its accidental implantation in eyes, mouth, or other anatomical areas where monkeypox virus infection might constitute a special hazard (e.g., the genitals or anus)



- Avoid contact with animals that could harbor the virus
- Avoid contact with any materials, such as bedding, that has been in contact with a sick animal.
- ▶ Isolate infected patients from others who could be at risk for infection.
- Practice good hand hygiene after contact with infected animals or humans.
- ► Use personal protective equipment (PPE) when caring for patients.

Immunization

- Two orthopoxvirus vaccines are available from CDC Drug Service for persons at risk for occupational exposure.
- JYNNEOS (also known as Imvamune or Imvanex) is a live, nonreplicating vaccine licensed by the FDA for prevention of smallpox and monkeypox disease in adults 18 years of age and older determined to be at high risk for smallpox or monkeypox infection.
- ACAM2000 is a live vaccine for active immunization against smallpox disease licensed by FDA for persons determined to be at high risk for smallpox infection.



Discovery of small pox vaccine

به نام خدا

37

سال 1264قمری، نخستین برنامهی دولت ایران برای واکسن زدن به فرمان امیرکبیر آغاز شد. در آن برنامه، کودکان و نوجوانانی ایرانی را آبلهکوبی میکردند اما چند روز پس از آغاز آبلهکوبی به امیر کبیر خبردادند که مردم از روی ناآگاهی نمیخواهند واکسن بزنند. بهویژه که چند تن از فالگیرها و دعانویسها در شهر شایعه کرده بودند که واکسن زدن باعث راه یافتن جن به خون انسان میشود!!!

هنگامی که خبر رسید پنج نفر به علت ابتلا به بیماری آبله جان باختهاند، امیر بیدرنگ فرمان داد هر کسی که حاضر نشود آبله بکوبد باید پنج تومان به صندوق دولت جریمه بپردازد. او تصور می کرد که با این فرمان همه مردم آبله میکوبند. اما نفوذ سخن دعانویسها و نادانی مردم بیش از آن بود که فرمان امیر را بپذیرند. شماری که پول کافی داشتند، پنج تومان را پرداختند و از آبلهکوبی سرباز زدند. شماری دیگر هنگام مراجعه مأموران در آب انبارها پنهان

روز بیست و هشتم ماه ربیع الاول به امیر اطلاع دادند که در همه ی شهر تهران و روستاهای پیرامون آن فقط سیصد و سی نفر آبله کوبیدهاند. در همان روز، پاره دوزی را که فرزندش از بیماری آبله مرده بود، به نزد او آوردند. امیر به جسد کودک نگریست و آنگاه گفت: ما که برای نجات بچههایتان آبلهکوب فرستادیم .پیرمرد با اندوه فراوان گفت: حضرت امیر، به من گفته بودند که اگر بچه را آبله بکوبیم جن زده میشود. امیر فریاد کشید: وای از جهل و نادانی، حال، گذشته از اینکه فرزندت را از دست دادهای باید پنج تومان هم جریمه بدهی. پیرمرد با التماس گفت :باور کنید که هیچ ندارم. امیرکبیر دست در جیب خود کرد و پنج تومان به او داد و سپس گفت: حکم برنمیگردد، این پنج تومان را به صندوق دولت بپرداز. چند دقیقه دیگر، بقالی را آوردند که فرزند از آبله مرده بود. این بار امیرکبیر دیگر نتوانست تحمل کند. روی صندلی نشوانست و با حالی زار شروع به گریستن کرد ...

در آن هنگام میرزا آقاخان وارد شد. او در کمتر زمانی امیرکبیر را در حال گریستن دیده بود. علت را پرسید و ملازمان امیر گفتند که دو کودک شیرخوار پاره دوز و بقالی از بیماری آبله مردهاند. میرزا آقاخان با شگفتی گفت عجب، من تصور میکردم که میرزا احمدخان، پسر امیر، مرده است که او این چنین هایهای میگرید. سپس، به امیر نزدیک شد و گفت عگریستن آن هم به این گونه، برای دو بچهی شیرخوار بقال و چقال در شأن شما نیست. امیر سر برداشت و با خشم به او نگریست، آنچنان که میرزا آقاخان از ترس بر خود لرزید. امیر اشکهایش را پاک کرد و گفت علیهای میرزا آقاخان از ترس بر خود لرزید. امیر داریم، مسئول مرگشان ما هستی را بر عهده آبله نکوبیدهاند

امیر با صدای رسا گفت :و مسئول جهلشان نیز ما هستیم. اگر ما در هر روستا و کوچه و خیابانی مدرسه بسازیم و کتابخانه ایجاد کنیم، دعانویسها بساطشان را جمع میکنند. تمام ایرانیها اولاد حقیقی من هستند و من از این میگریم که چرا این مردم باید این قدر جاهل باشند که در اثر نکوبیدن آبله بمیرند ...

روحش شاد

Orthopoxvirus Vaccine Guidance for Persons at Risk for Occupational Exposure

On November 2021, the Advisory Committee and Immunization Practices (ACIP) <u>voted to recommend</u> vaccination for select persons at risk for occupational exposure to orthopoxviruses. Such persons include:

- Research laboratory personnel, clinical laboratory personnel performing diagnostic testing for orthopoxviruses, and for designated response team members at risk for occupational exposure to orthopoxviruses.
- Healthcare personnel who administer ACAM2000 or care for patients infected with replication competent orthopoxviruses based on shared clinical decision-making.



- Persons who are at continued risk for occupational exposure to more virulent orthopoxviruses like Variola virus or monkeypox virus should receive booster doses of JYNNEOS every 2 years after the primary JYNNEOS series.
- Persons who are at continued risk for occupational exposure to replication competent orthopoxviruses like vaccinia virus or cowpox virus should receive booster doses of JYNNEOS at least every 10 years.
- Persons who are at continued risk for occupational exposure to orthopoxviruses, and who received an ACAM2000 primary vaccination, should receive a booster dose of JYNNEOS as an alternative to a booster dose of ACAM2000.



- Dr. Rosamund Lewis, head of WHO's smallpox department, said that "there is no need for mass vaccination," explaining that monkeypox does not spread easily and typically requires skin-toskin contact for transmission.
- No vaccines have been specifically developed against monkeypox, but WHO estimates that smallpox vaccines are about 85% effective.



- Smallpox vaccination was discontinued worldwide in the 1980s and cases of monkeypox in Africa were comparatively small before this.
- This increase in numbers in this age group might reflect the loss of cross-protective immunity to monkeypox from not receiving the smallpox vaccination.





Primary Vaccination Site Reaction



Difference between the smallpox vaccine and BCG scars

- The smallpox vaccine was not widely distributed in the United States after 1972. If a person was born after this time, their vaccine scar is likely a BCG scar.
- Although scarring types can vary, a BCG scar tends to be raised and slightly rounded.
- A smallpox scar tends to be depressed, or below the skin. It's slightly rounded, with jagged edges.

Treatment of Monkeypox

- Currently there is no specific treatment approved for monkeypox virus infections.
- Antivirals developed for use in patients with smallpox may prove beneficial.



- Tecovirimat (also known as TPOXX) is an antiviral medication that is <u>approved by FDA</u> for the treatment of human smallpox disease in adults and pediatric patients weighing at least 3 kg.
- CDC allows the use of Tecovirimat for the treatment of non-variola orthopoxviruses (including monkeypox) in an outbreak.
- Tecovirimat is available as oral (200 mg capsule) and injection for intravenous formulations (mixing its content with semi-solid food for pediatric patients)



- Cidofovir (also known as Vistide) is an antiviral medication that is <u>approved by the FDA</u> for the treatment of <u>cytomegalovirus</u> (CMV) retinitis in patients with AIDS.
- CDC allows for the use of Cidofovir for the treatment of orthopoxviruses (including monkeypox) in an outbreak.



- Vaccinia Immune Globulin Intravenous (VIGIV) is <u>licensed by FDA</u> for the treatment of complications due to vaccinia vaccination including eczema vaccinatum, progressive vaccinia, severe generalized vaccinia, vaccinia infections in individuals who have skin conditions, and aberrant infections induced by vaccinia virus (except in cases of isolated keratitis).
- CDC allows the use of VIGIV for the treatment of orthopoxviruses (including monkeypox) in an outbreak.



- Brincidofovir (also known as Tembexa) is an antiviral medication that was <u>approved by the FDA</u> on June 2021 for the treatment of human smallpox disease in adult and pediatric patients, including neonates.
- CDC is currently developing an EA-IND to help facilitate use of Brincidofovir as a treatment for monkeypox
- State and territorial health authorities can direct their requests for medical countermeasures for the treatment of monkeypox to the CDC Emergency Operations Center (770-488-7100).

Mortality

- ► The illness typically lasts for 2-4 weeks.
- In Africa, monkeypox has been shown to cause death in as many as 1 in 10 persons who contract the disease.
- Since 2017, the few deaths of persons with monkeypox in West Africa have been associated with young age or an untreated HIV infection
- No deaths have been reported in nonendemic countries



The antiviral tecovirimat for treatment of seriously ill monkeypox cases, and the third-generation smallpox vaccine Imvanex (Bavarian Nordic, Hellerup, Denmark) for use as prophylaxis in all close and high-risk case contacts, together with specific guidelines for their use, need to be made available urgently universally at affordable cost.