IADVL Academy Position Statement on Emerging Dermatoses in India: Monkeypox

Abstract

As we were on the road to recovery from the coronavirus disease-19 (COVID-19) pandemic, the world is waking up to yet another potential adversary. Monkeypox (or human monkeypox) caused by monkeypox virus (an orthopox virus) is fast emerging in more than 80 countries worldwide, where it has never been historically reported. We in India, have already seen the advent of this outbreak since July 2022, with a progressive rise in number of cases being seen. Though the virus is not a novel virus; it is presenting with atypical manifestations as compared to our conventional knowledge of the disease. Through this document, the Indian Association of Dermatologists, Venereologists, and Leprologists Academy aims to sensitize dermatologists toward recognizing the clinical features and responding promptly, to contain the outbreak at the earliest. In view of the non-availability of specific antiviral drugs as well as vaccines; early detection, isolation, and prevention of spread form the mainstay of our approach towards the outbreak, which has been declared to be a "Public Health Emergency of International Concern" by the World Health Organization.

Keywords: *Diagnosis, India, monkeypox, monkeypox virus, prophylaxis, treatment, World Health Organization*

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Access this article online

Website: www.idoj.in

DOI: 10.4103/idoj.idoj_437_22

Quick Response Code:

Introduction

As we recovered from the deadly wave of COVID-19 pandemic, caused by the Delta variant, the second half of 2022 has presented us with another potential threat in the form of monkeypox. It is a viral infection caused by monkeypox virus (MPV) a double-stranded DNA virus belonging to the group Orthopoxviruses. It was largely considered an endemic zoonotic infection for years; however, now human-to-human transmission and occurrence in naive population is being increasingly documented. The name "monkeypox" is considered a misnomer as monkeys are neither the origin nor the reservoir of the virus. Though its origin is largely unknown, several rodents and small mammals are known to harbor MPV.[1] With 43 years gone by since smallpox vaccination was discontinued, we now have a substantial pool of susceptible population world over and in India. In addition, the overarching issues of overcrowding, poor hygienic conditions, malnutrition, parasitic infestations, and unsafe sexual practices seem to play an important role in its spread.

Monkeypox, an emerging viral infection with prominent cutaneous findings, has been declared a "Public Health Emergency of International Concern" by the World Health Organisation (WHO) on July 23, 2022.[2] As most dermatologists have not commonly seen it, the Indian Association of Dermatologists, Venereologists, and Leprologists (IADVL) Academy compiled this document with an aim to familiarize them with its presentation and management. Most of the cases of monkeypox are diagnosed based on the characteristics of the skin rash; hence, dermatologists need to be sensitized regarding the same. This article aims to present an updated overview of this ongoing outbreak, in the context of existing knowledge. It is important for health care workers (HCW) to update their knowledge regarding its prevention, management and prophylaxis, to effectively contain its spread, as well as to protect themselves. We hope that this document will serve as a primer for dermatologists presented with a situation where the need to identify monkeypox and differentiate it from other skin rashes arise. This document reflects

How to cite this article: Jindal R, Grover C, Sarkar R, Gupta LK. IADVL academy position statement on emerging dermatoses in India: Monkeypox. Indian Dermatol Online J 2022;13:559-69.

Received: 10-Aug-2022. **Revised:** 12-Aug-2022. **Accepted:** 14-Aug-2022. **Published:** 05-Sep-2022.

currently available knowledge; however, the scenario is fast evolving and further changes may occur with increasing research.

History of Evolution

MPV was first isolated in 1958 in monkeys transported from Africa to Copenhagen.[1] Despite this nomenclature, it is now known that rodents including squirrels, rats, and small mammals form the largest animal reservoirs of MPV. A 9-month-old child from Democratic Republic of Congo (DRC) was the first human case identified in August 1970. Since then small outbreaks have been reported infrequently in central and western African countries.[3]

Initially, the disease remained confined to endemic African countries, with DRC reporting the maximum number of cases. However, since the turn of the century, limited outbreaks outside of endemic regions have been reported. These include the United States in 2003–2004, in 2013 (47 cases) and Nigeria in 2017–2018 (over 80 cases).[4] The situation dramatically escalated from May 2022, with much larger numbers being reported from many non-endemic countries with a travel link to Europe and North America. The current outbreak is mainly centered in European countries, and the Western hemisphere.[2] India was the first country to report a case in the South-East Asian Region, with travel links to the middle-east region.[5] It is currently unclear as to when and why this outbreak began, but the effects are now widespread. As on August 16, 2022, there were 38019 cases worldwide, in 93 countries (of which 86 had never reported monkeypox historically).[6]

Evolution in India

The first case documented in India was from Kerala, reported on July 15, 2022. Infact, this was the first case reported from the whole WHO South-East Asian Region.[5] It was reported in a 35-year-old man with travel history from the middle-east. By mid-August, 2022, there were nine cases in India, with many more suspected cases.[7] On 1st August, India confirmed its first monkeypox death, that too in a patient who had travelled back from middle-east.[8] The Indian scenario is fast evolving and ever changing by the time this article was compiled. Dedicated isolation and observation rooms have been, and are being identified across the country and in various hot-spots. Confirmatory testing, initially being done in the National Institute of Virology, Pune, was started in AIIMS (Delhi), and is now available in 15 different specialized laboratories with an aim to make it available more widely and to reduce the testing time.[9] Guidelines on management of monkeypox disease were issued by the Ministry of Health and Family welfare, Government of India (MOHFW-GOI) on 31st May, 2022.[10]

Etiology

MPV belongs to the family Poxviridae, subfamily Chordopoxviridae, and genus Orthopoxvirus. Orthopox viruses are large, double-stranded DNA viruses, residing in many hosts including rodents, rabbits and small primates. It has been circulating as a zoonosis for long, with human cases being reported occasionally as spill-over infections. The genus Orthopoxviruses contains 12 species, of which the most well-known is the variola virus, responsible for smallpox. Smallpox was eradicated globally in 1977, primarily through increased vaccination coverage. Other diseases caused by orthopoxviruses included cowpox, horsepox, camelpox, molluscum contagiosum, and so on, with the most recently described disease being Alaskapox (reported in 2015).[11] Evolution of orthopoxviruses has entailed progressive loss of genes, leading to better virus survival, evasion of host immunity, changing transmission, and clinical features.[12] The virus may be becoming more adapted to humans.[13]

MPV is known to have two distinct clades. The Central African (Congo Basin) clade is considered more virulent, and causes more severe disease, with greater morbidity, mortality (up to 10%) and viremia.[4] It was responsible for the 2003–2004 outbreak in the United States with human-to-human transmission. The West African clade, with reduced virulence, is considered less severe with lesser mortality rates (3.6%). In the current outbreak, it is being proposed that the MPV responsible possibly belongs to clade 3, (West African clade lineage B.1) which clusters with 2018–2019 cases. It still seems to segregate in a divergent phylogenetic branch.[14] This may be a result of continuous accelerated evolution. MPV is resistant to destruction by ether or drying. It is susceptible to chloroform, methanol, formalin, and heating at 56°C (30 mins).[15]

Orthopoxviruses are known to be dangerous pathogens, as reflected by the scourge of smallpox, which caused massive fatalities throughout recorded human history. Even the smallpox virus is presumed to have evolved from a rodent orthopoxvirus; serving as a grim reminder towards the potential danger posed by monkeypox resurgence. With continuing deforestation, and altered environments, zoonoses continue to adapt to human hosts, as reflected by the COVID-19 pandemic. Coming on its heels, the monkeypox epidemic should be taken seriously, considering our poor herd immunity. Orthopoxviruses exhibit considerable cross-reactivity and cross-protection; thus, infection with any member of the genus confers some protection from another member.

Epidemiology

It is presumed that monkeypox has been occurring in Sub-Saharan Africa for thousands of years, though not recognized as a distinct disease till 1970.[15] The slow

disappearance of smallpox highlighted its distinctive features. The virus was laboratory identified in 1958 in State Serum Institutes in Copenhagen, Denmark, and Africa.[1] Though, clusters of cases continued to be reported from Africa, widespread smallpox vaccination probably kept it under check for many years. However, this temporary control is now largely waning. The ongoing civil war in endemic areas, with increased deforestation, hunting for food and increased animal contact have probably contributed to its resurgence.

The disease assumed global public health importance in 2003, when clusters were reported outside of an endemic area, that is in the US mid-west region. This outbreak was traced to contact with pet prairie dogs kept with exotic rodents imported from Ghana.[16,17] Since then, sporadic cases or clusters have been reported, with the largest one (excluding the 2022 scenario) being from Nigeria in 2017.[18]

Epidemiologically, the R0 (reproductive ratio) value for monkeypox in areas where there is negligible exposure to Orthopoxviruses, is estimated to be 0.8–1.0 while being higher in certain populations, even up to 1.8.[2,15] This indicates a high degree of transmissibility of the disease, pointing toward an imminent epidemic, if special measures are not taken to social distance and quarantine infected individuals.

Certain epidemiological features of the current epidemic are atypical, unique, and noteworthy.

- The infection is prevalent among individuals less than 40 years of age, with a median age of 31 years.[18] This is possibly due to the unimmunized segment of population. Conventionally, monkeypox used to be a disease of the children; however, its mean age of incidence has been rising over the past decades.
- A higher prevalence is being seen in males. The exact reasons for the same may not be known; however, higher detection rates as well as higher chances of travel may be responsible.
- The disease is being reported in sexual contacts of infected individuals. However, it is not clear, whether MPV is sexually transmitted or the spread occurs only due to close contact.
- The disease is being seen more commonly in men having sex with men (MSM) or those who identify themselves as gay and bisexual. The significance of this finding and its reflection on modes of transmission remains under research. Though the virus has been isolated from semen, the implications may take time to establish.[19,20]

Modes of Transmission

Even though the exact mode of transmission is still under investigation, several possibilities have been proposed; all have an association of contact with infected animals or infected humans. These are summarized in Table 1. The human-to-human transmission was considered less common than animal-to-human transmission, but the current outbreak is fueled by the former. The most common mode for human transmission was considered through respiratory droplets; however, sexual transmission is being actively investigated.[15,21]

Transmission in healthcare settings

The risk of transmission of monkeypox in healthcare settings, outside of endemic regions is not well defined. Transmission to HCW or to other patients had been characterized well in endemic settings, but these happened to be resource poor all along. A review of published reports from 2000 to May 2022 (excluding the current global outbreak), found a single reported transmission event in a non-endemic region. The study concluded that transmission to HCW seems to be rare with adequate personal protective equipment (PPE) and hand hygiene.[22] Nevertheless, the extent of exposure, and risk stratification need to be defined. Adequate PPE as well as pre-exposure prophylaxis (PrEP) in the form of vaccines, is recommended for the following occupational groups

- Frontline workers or members of the medical response team, engaged in patient care and sample collection

Table 1: Proposed modes of transmission of human monkeypox

Mode	Source
Animal to human transmission (primary mode)	Direct contact with or exposure to an infected animal
	Bites or scratches
	Most commonly due to body fluids like saliva, respiratory secretions
	Exudate from cutaneous/mucosal lesions
	Exposure to faces of an infected animal
	Hunting, cooking, or consumption of infected animals
	Now human to animal transmission is also being suspected
Human to human transmission (secondary transmission)	Close contact
	Respiratory droplets in cases with prolonged face-to-face contact
	Direct contact with lesions
	Recently contaminated objects/surfaces like bedding, dishes or utensils of infected individual
Sexual transmission?	Not confirmed as per WHO
	Transmission can be attributed to close contact
	It can also be due to semen/vaginal fluid (not confirmed yet)
Vertical transmission?	Mother to child transmission during pregnancy (through placenta)
	More reports needed

- Laboratory personnel working with or performing diagnostic testing for Orthopoxviruses
- HCW who administer the live vaccinia vaccine
- All categories of HCW involved directly in patient care responsibilities.

Adequate PPE as per MOHFW-GOI guidelines includes long-sleeved gown, N95 mask, gloves, and eye protection (face-shield or goggles).[10] Standard donning and doffing precautions should be followed to prevent contamination. Potentially contaminated surfaces should be cleaned with 1% hypochlorite solution (or equivalent). Attempt should be made to minimize aerosol generation when dealing with patient bedding, clothes and so on. All waste should be disposed off as per bio-medical waste (BMW) management rules. Hand hygiene should be ensured at all steps. No guidelines for vaccination of HCW exist from the Government of India.

Clinical Features

Conventionally, monkeypox has been a mild and self-limiting disease, with resolution of cutaneous lesions in 2–4 weeks. However, children, pregnant women, and immunocompromised persons can develop severe disease with complications.[23] WHO reported skin rash (localized/generalized) as the most frequent symptom in 16,016 patients reported till July 22, 2022. This was followed by fever, lymphadenopathy, fatigue, headache, and muscle aches.[24]

Typically, an incubation period of 5–21 days (most frequently 7–14 days) from the day of infection, is followed by a prodrome of fever, chills, headache, muscle aches, sore-throat, and fatigue. Symptoms are nonspecific, and may not be taken seriously. This phase is generally associated with lymphadenopathy that lasts for 1–5 days [Figure 1].[23]

The prodrome is followed by an enanthem in the form of oral ulcers on tongue and buccal mucosa. They can be quite symptomatic and compromise oral intake. It is closely followed by an exanthem within 24 hours. The hallmark of monkeypox is a disseminated vesico-pustular rash. However, in the current outbreak, more localized exanthem is seen, appearing even without a prodrome. The cutaneous lesions start as macules, progressing to papules, vesicles, and pustules over a period of 3–6 days. The pustules commonly develop central umbilication and heal with scab formation, which falls off in 7–14 days, leaving behind hypopigmented or hyperpigmented pitted scars [Figure 2a, b]. Typically, the lesions are monomorphic, exhibiting a centrifugal distribution, with predilection for mucosae (oral and genital) and extremities (palms and soles). The number of lesions can vary from 10 to over 500 with size ranging from 0.5 to 2.5 cm. The lesions are initially painful, become pruritic once

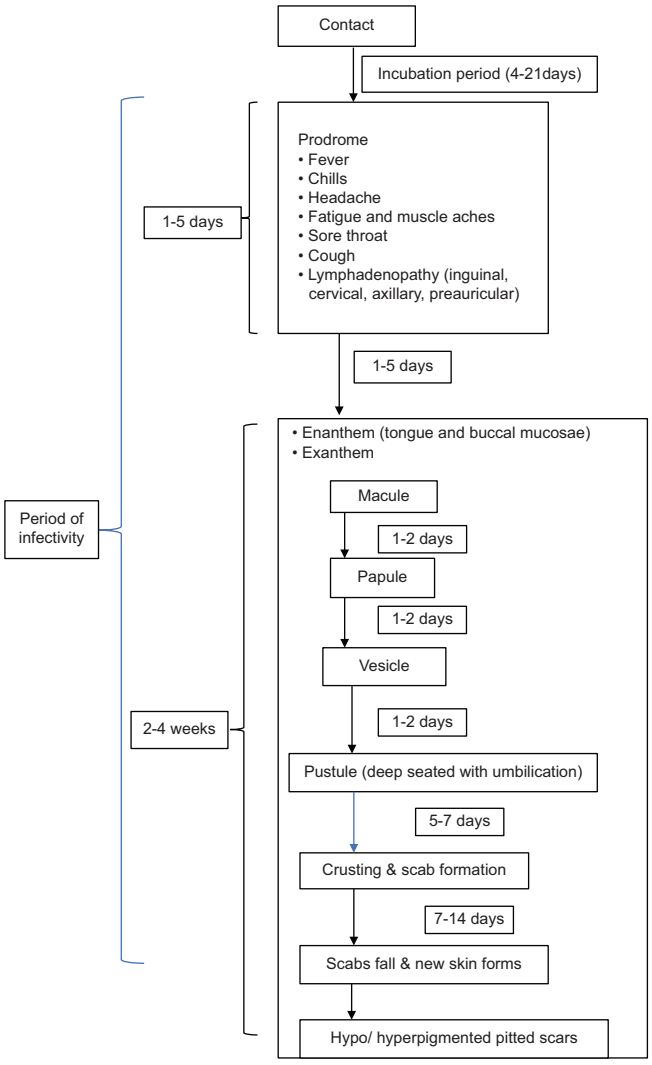

Figure 1: Clinical course of monkeypox infection

healing starts.[4,23,25] The patient is deemed infectious from the start of symptoms until all scabs have fallen off with epithelialization [Figure 1].[24]

In the current multicountry outbreak, atypical presentations of monkeypox are being described [Table 2].[24,26] Awareness regarding these features can help suspect and diagnose cases better. The reasons for these atypical presentations could be many, including immunocompromised hosts, altered modes of entry, poor orthopoxvirus immunity, alterations in the virus, and involvement of naive population subsets.

Complications

These include secondary bacterial infections and cellulitis; bronchopneumonia and respiratory distress; sepsis and septic shock; and encephalitis. These are associated with both increased morbidity and mortality. Corneal infection, conjunctivitis, and keratitis can lead to corneal scarring and vision loss. However, data regarding the timeframe of development of complications and their

incidence is lacking, even though it largely appears to be a mild and self-limiting illness.[27]

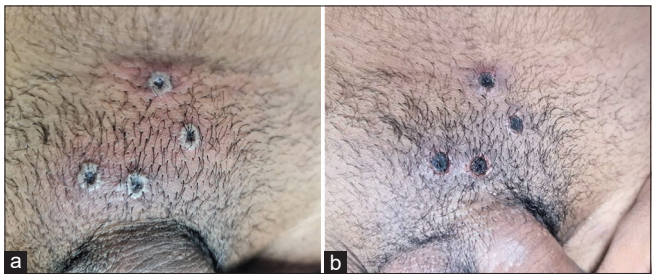

Figure 2: Typical lesions of monkeypox present on the genital area in a male patient (a). The lesions crust over a period of 7 days (b).[Image courtesy Dr Ramesh TC, Consultant Dermatologist, Sharjah, United Arab Emirates]

Historically, the mortality associated with monkeypox has been 1%–10% cases, being higher with the Central African clade.[4] The West African clade, has been associated with less mortality, though morbidity is still noticeable. In preliminary data analysis, mortality risk has been found to be 0.4%–4% for the present outbreak, with no deaths being reported in two large series.[6,19,20,28] As with other resurging infections, the media hype, scare as well as stigma associated with the infection are also taking their toll; hampering prompt reporting and effective containment of the spread.

Differential Diagnosis

The clinical differentiation of monkeypox rash from disseminated herpes simplex virus infection, varicella,

Table 2: Atypical presentations reported in 2022 monkeypox multi-country outbreak

Differences seen in Monkeypox 2022	Atypical features seen
Differences in epidemiology	Human-to-human transmission (earlier not seen with West African clade, which was animal to human transmission)
	Involvement of adults, not children (earlier it was a disease of children)
	Male predilection (>90%)
	Detected more in patients who identify themselves as gay, bisexual, and MSM
	Most spread reported with sexual contact; however, up to 20% patients have reported no previous sexual contact (suggesting an asymptomatic group, or fomite transmission)
	Correlation with high risk sexual behavior
	Poor correlation with HIV status or vaccination status
Differences in clinical presentation	Mild to absent prodrome
	Few localized lesions or even a single lesion
	Rash beginning in genital area. Initial presentation as a genital/perianal rash
	Preferential involvement of oral and genital mucosae. Mucosal "chancriform" ulcers
	May not involve face or extremities at all
	Starts as localized homogenous papules, in area of inoculation (called "pseudopustules" instead of pustules, similar to other orthopoxvirus lesions)
	Initial papular lesions at entry site, followed by distant pustular lesions
	Generalized small pustules may appear in some of the patients
	Monkeypox "whitlow" described in many cases
	Involvement of palms and soles
	Lesions can be seen in different stages of development (pleomorphic/heterogenous/asynchronous) rather than the early monomorphic rash
	Lesions preceding prodromal symptoms (fever)
	A small subset of patients presenting without skin lesions, but with anal pain and bleeding (proctitis).
	Macular (morbilliform) eruption in 6% patients
Differences in outcome	Mostly a mild, self-limiting illness.
	Hospitalization for various reasons required in up to 13% patients
	Antiviral treatment administered in <5%
	Average age of death 27 years (earlier occurred in children <10 yrs)
	At 4% mortality (early data), the rates are less than Central African clade and comparable with West African clade.
	Much lower rates of mortality (0.4%) also suggested, but not conclusively proven
Stigma attached	Current outbreak being viewed as an STI (Sexually Transmitted infection)
	High possibility of co-existence of other STI's; patients should be thoroughly evaluated
	However, monkeypox is no more a "Gay disease" than it is an "African disease"[20]

molluscum contagiosum, hand-foot-mouth disease (HFMD), and secondary syphilis can be quite challenging. This is compounded by a heightened awareness, anxiety, lack of information, and atypical presentations. The cutaneous lesions in herpes group of viruses are in the form of small vesicles and dissemination occurs in the setting of immunosuppression. Molluscum contagiosum typically affects children and presents with hard, pearly-white, umbilicated papules. The real clinical confusion as of now is being reported with varicella (Varicella Zoster Virus [VZV]) and HFMD (Coxsackie A16 most commonly). The clinical differentiation points are enlisted in Table 3. The presence of lymphadenopathy is considered to be an important differentiating feature as it develops early in monkeypox.[29]

Diagnosis

The diagnosis of monkeypox is based on WHO Surveillance case definition [Table 4]. It categorizes patients into suspected, probable, and confirmed. All suspected cases should be tested for diagnostic confirmation. However, since clinical differentiation from other causes of vesiculo-pustular lesions is difficult, the decision to test should be guided by both clinical and epidemiological factors. A high index of suspicion and thorough knowledge about atypical manifestations can help suspect a case. The MOHFW-GOI endorses a period of observation of 21 days for all asymptomatic travelers returning from outbreak/ endemic regions.[10] For all suspected symptomatic cases, samples need to be sent to Indian Council of Medical Research-National Institute of Virology (ICMR-NIV), Pune or the designated Virus Research and Diagnostic Laboratories (VRDL) for confirmation [Figure 3].[9] Table 5 describes the specimen collection and the transport requirements as per MOHFW-GOI.[10]

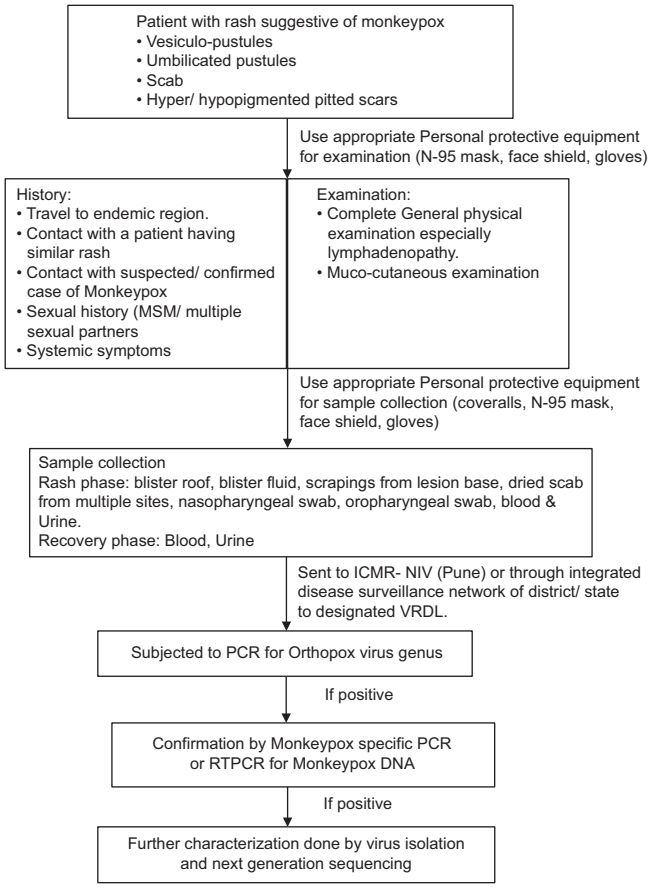

Figure 3: Management flowchart for suspected cases with monkeypox

Table 3: Clinical characteristics of monkeypox as compared to Varicella and HFMD

Clinical feature	Monkeypox	Varicella	Hand-foot-mouth disease (HFMD)
Typical lesion morphology	Classic monkeypox shows vesiculo-pustules with deep central umbilication and peripheral rim of erythema	Vesicles on an erythematous base (dew-drops on rose petals)	Gray oval vesicles
	Size varies from 0.5 to 2.5 cm	Size varies from 0.2 to 0.4 cm	Size varies from 0.2 to 0.4 cm
	Monomorphic lesions	Polymorphic lesions	Monomorphic lesions
	Scab falls off leaving behind hypo/ hyperpigmented pitted scars	Scab falls off leaving behind hyperpigmentation. Only some patients develop scars.	Heal with desquamation
	Lesions are painful initially	Lesions are often itchy.	Generally asymptomatic
	Later become pruritic		
	However, atypical presentations are being noted as described in Table 2. These may be the predominant presentations in the current outbreak.		
Lesion distribution	Centrifugal distribution	Centripetal distribution	Palms, soles and oral mucosae preferentially involved
	Starts from oral cavity and progresses to involve genitalia and extremities	Trunk and proximal extremities predominantly involved	Few lesions over buttocks
	Usually single crop of lesions	Multiple crops of lesions	
Systemic features	Prodrome of fever, malaise, muscle ache,	Mild prodrome	Sometimes a prodrome of fever
	Cough, sore throat, nausea, vomiting, diarrhea	Fever, sore throat and cold	
	Commonly associated with lymphadenopathy		

Table 4: WHO surveillance case definition for monkeypox

Case category	Case definition	Additional qualification for diagnosis
Suspected case	Person of any age	AND having one or more of the following
	Having history of travel to an affected country within last 21 days	Headache
		Fever (>38.5°C)
	Presenting with an unexplained acute rash	Lymphadenopathy
		Myalgia
		Back pain
		Asthenia
Probable case	Meeting the definition of a suspected case	And having an epidemiological link with a probable or confirmed case of Monkeypox within 21 days of symptom onset, in the form of
	With Clinically compatible illness	Prolonged face to face exposure (Including HCW with or without appropriate PPE)
		Direct physical contact with skin or skin lesions
		Sexual contact
		Contact with contaminated clothing, bedding, or utensils
		ADDITIONAL LINKS
		Multiple/anonymous sexual partners within 21 days of symptom onset.
		Detectable level of antiorthopoxvirus IgM antibody (4-56 days after rash)*
		Four-fold rise in IgG anti-orthopoxvirus antibodies in paired samples (acute up to 7 days and convalescent Day 21 onwards)*
		Positive orthopoxvirus specific PCR without monkeypoxvirus specific PCR or sequencing
Confirmed case	Laboratory confirmed monkeypox virus by detection of unique sequence of viral DNA by RTPCR/sequencing	

*in the absence of smallpox/monkeypox vaccination

Table 5: Recommendations for specimen collection and transport in suspected case of Monkeypox

Specimen collection (Appropriate PPE must be worn)			Sample transport
Rash phase		Recovery phase	
Lesion fluid aspirated with intradermal syringe	From multiple sites	Blood collected in SSGT	All samples must be kept at+4°C immediately post collection
Lesion roof	To be sent in screw-capped plain tubes		
Lesion base scrapings			Serum tube should be centrifuged before shipment
Lesion crust			
Nasopharyngeal/Oropharyngeal swab	In dry plain tubes	Urine in sterile container	All samples are labeled and sealed with parafilm and wrapped in absorbent tissue paper/cotton and packed in a zip lock bag.
Blood collected in SSGT (yellow top)	Plain vial		Samples are to be transported in dry ice along with case record form.
Blood collected in EDTA (purple top)	EDTA vial		The form should be packed outside of the triple layer closure of patient samples.
Urine collected in sterile container			

SSGT- Serum separating gel tube, EDTA- Ethylene diamine tetra-aceitic acid tube

Management

A suspected or confirmed case should be managed in an isolation room (with separate ventilation) at hospital or in-home setting. MOHFW-GOI has issued a standard Case Report Format for reporting such a case and submitting samples for testing.[10] Currently, reporting to the District Surveillance Officer is required with the list of State Surveillance Officers being available from Integrated Disease Surveillance Program (IDSP) website.[30] The samples can be sent to the 15 designated VRDL across the country.[9]

During the "rash phase" sampling is to be done from lesion roof, lesion fluid, and lesion base scrapings, in addition to nasopharyngeal and oropharyngeal swabs, blood, and urine [Table 5]. Highest diagnostic yield is expected from lesional sampling. However, during the recovery phase, serum samples are to be collected.[10]

Patient should wear a triple-layer mask to prevent transmission to the HCW or to household contacts. Lesions should be kept covered with appropriate clothing. HCW and close contacts must themselves wear appropriate PPE and follow hand-hygiene practices. The period of isolation is continued until all scabs fall and the reepithelialization has occurred.

Most infections, being mild, can be managed appropriately with supportive care and symptomatic management [Table 6]. However, for complications, expert advice must be sought and patients should be managed by a multispecialty team. Managing the fluid-electrolyte balance and nutritional needs of the patient is of utmost importance, considering decreased oral intake because of painful oral ulcers. Similarly, genital lesions need adequate cleaning to avoid secondary bacterial infection. Symptomatic management for fever, gastrointestinal symptoms, conjunctivitis, and pruritus form the mainstay of therapy. Predisposed individuals including children, pregnant women and immunocompromised persons should be monitored regularly for early detection of complications. "Danger signs" include pain in eye, blurring of vision, shortness of breath, chest pain, altered consciousness, decreased urine output, poor intake, or lethargy.

There are no USFDA-approved antivirals against MPV. Thus, specific management with antiviral drugs is not routinely recommended. However, cidofovir, brincidofovir, and tecovirimat have been shown to have antiviral activity against MPV and can be potential options in the future.[31] Of these, tecovirimat, an antiviral drug approved by USFDA for use in children and adults with smallpox, has shown safety in clinical trials; though efficacy data is limited. Indications for antiviral treatment are summarized in Table 7.[32] Currently, none of these drugs is available in India.

Pre- and post-exposure prophylaxis

The role of Vaccinia Immune Globulin Intravenous (VIGIV) and vaccinia virus-based vaccines are being explored for offering pre- and postexposure prophylaxis. However, this will depend on continuous availability of stocks if the need arises. These are currently unavailable in India.

VIGIV was approved for the management of complications following vaccination with vaccinia virus vaccine.[33] It is currently under investigation for emergency use in the treatment of monkeypox.

There are no specific vaccines for MPV.[29] Historically, studies conducted in DRC in 1980 reported a protection of 85% against monkeypox in those vaccinated for smallpox (1st generation or Dryvax vaccine).[34] Based on this premise, currently two potential vaccines are being proposed. These are the 2nd generation ACAM2000™ (live replication competent vaccinia virus-based vaccine) (single percutaneous dose

Table 6: Management protocol for patients suspected/diagnosed with monkeypox

Supportive management	Symptomatic management	Specific management
General care	Antipyretics for fever	**Antiviral drugs***
Adequate hydration and nutritional support	Antihistamines for pruritus	**Cidofovir:** 5 mg/kg per dose weekly for two or more doses (with probenecid)
Maintenance of fluid-electrolyte balance	Antiemetics for nausea and vomiting	**Brincidofovir:** 4 mg/kg per dose weekly for two doses
Cutaneous lesions	**Management of complications**	**Tecovirimat:** to be given for 14 days
Cleaning of lesions	Secondary bacterial infection-consider oral antibiotics	Intravenous (200 mg twice daily for 35-119 kg, 300 mg twice daily≥120 kg)
Topical antibiotics	**Appropriate referrals and multispecialty management**	Oral (600 mg twice daily for 40-119 kg, 600 mg thrice daily≥120 kg)
Covering with clothes/gown/light dressing	Respiratory distress and pneumonia (Pulmonologist)	
Genital lesions	Eye pain and decreased vision (ophthalmologist)	
Cleaning	Vomiting and diarrhea (gastroenterologist)	
Sitz bath	Encephalitis (neurologist)	
Oral ulcers	Sepsis (intensivist)	
Soft and bland diet	**Consider co-infection with other STI's if the setting suggests so**	
Topical anti-inflammatory and anesthetic gels	Coinfection with HIV leads to larger skin and genital ulcers	
Eye (conjunctivitis and keratitis)	Consider gonorrhoea, chlamydia, herpes, syphilis, etc., and mange accordingly.	
Lubricating eye drops		
Antibiotic eye drops		
To prevent catastrophic eye damage		

*None of these drugs were developed for MPV. Cidofovir is USFDA approved for CMV retinitis in patients with AIDS. Brincidofovir and Tecovirimat are approved for smallpox

Table 7: Indications for antiviral therapy in monkeypox

Patient/ Disease characteristics	Alarming features
Serious disease	Hemorrhagic disease
	Confluent lesions
	Sepsis
	Encephalitis
	Disease requiring hospitalization
	Painful lymph nodes causing dysphagia
Immunocompromised host	HIV/AIDS
	Tumors/malignancy
	Transplant recipients
	Radiotherapy patients
	Patients on high dose corticosteroids
Pediatric patients	Especially those<8 years
Pregnant or breastfeeding women	
Skin disease	H/O Allergic dermatitis
	Active exfoliative skin disease like burns, chicken pox, herpes simplex infection, etc
Complications	Secondary bacterial skin infection
	Bronchopneumonia
	Concurrent diseases, other comorbidities
Abnormal MPV infection	Accidental implantation into eyes, mouth, genitals, anus etc., where MPV may pose special hazards
Altered laboratory parameters	Elevated transaminases or blood urea nitrogen
	Low serum albumin
	Elevated leucocyte count or low platelet count

administered with multiple punctures, to be repeated at 3 years) and 3rd generation JYNNEOS™ (nonreplicating modified vaccinia virus-based vaccine) (two doses, given subcutaneously, 4 weeks apart). Of these, JYNNEOS™ appears a favored option, considering the risk of reactivation of the virus with ACAM2000™, which could result in progressive vaccinia, eczema vaccinatum, and myopericarditis in patients who are immunocompromised or have a pre-existing condition like atopic dermatitis.[35] Pre-exposure vaccination for HCW working with MPV and managing patients and post-exposure prophylaxis with vaccine is being considered for high-risk contacts of confirmed cases.

"Ring vaccination" is encouraged to contain the outbreak, like it did for Ebola. It involves vaccinating family members, and close contacts of a confirmed case.[36] This might not be easy to apply in the present scenario, but may evolve as a strategy later.

Prevention of spread

Contact tracing and surveillance play an essential part in the containment of this outbreak. The aim is to check disease transmission, identify at-risk population, and institute appropriate treatment where required. Both backward and forward contact tracing is mandatory, to help find the source of infection as well as prevent spread.[10]

All the contacts of a probable or confirmed patient should be observed for 21 days after last contact with the index case (forward tracing) for development of any symptoms. However, quarantine or work exclusion is deemed unnecessary in asymptomatic contacts or HCW.

All close contacts within the last 21 days should also be examined for disease sequelae including scars. Confirmation can be done by testing for IgM antibodies against orthopoxvirus.[10] This helps in collecting useful epidemiological data.

Risk stratification, as suggested by WHO, categorizes contacts into high, intermediate, and low risk.[2]

- **High-risk exposure**: Direct contact of broken skin with the patient's lesions, mucosa or body fluid. Close proximal contact including face-to-face contact and sexual contact
- **Intermediate-risk exposure**: Direct contact of intact skin with a patient's lesion, mucosa or body fluid and non-direct but close contact without appropriate PPE also belongs to this category.
- **Low-risk contact**: If proper PPE is worn, then the risk is considered low.

Just as with COVID-19 pandemic, stringent hand-hygiene and appropriate use of PPE appears essential in prevention of transmission of monkeypox.

Useful resources

As the situation is fast evolving, dermatologists should keep abreast of the latest developments. Some useful online resources are summarized in Table 8. These are updated from time to time.

Conclusions

HCW are faced with another formidable adversary in the form of monkeypox. However, armed with knowledge acquired over the past 3 years, we are in a better position to combat the spread and minimize the consequences. PPE and hand hygiene continue to play a pivotal role in preventing its spread. The well-oiled surveillance machinery with heightened awareness alongwith targeted research in the field may help us contain monkeypox effectively. Nevertheless, we need to be aware of the atypical features, and unclear modes of transmission to consider all possibilities and be prepared as the epidemic evolves.

Financial support and sponsorship

Nil.

Table 8: Useful online resources to keep abreast of the evolving outbreak (Last accessed 12th August 2022

Title	Available from
Monkeypox outbreak Toolbox.	https://www.who.int/emergencies/outbreak-toolkit/disease-outbreak-toolboxes/monkeypox-outbreak-toolbox.
Monkey pox.	https://www.cdc.gov/poxvirus/monkeypox/index.html.
2022 Monkeypox outbreak Global Map.	https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html.
Monkeypox outbreak 2022.	https://www.who.int/emergencies/situations/monkeypox-oubreak-2022.
WHO India.	https://www.who.int/india/.
Guidelines on the management of Monkeypox disease.	https://main.mohfw.gov.in/diseasealerts-0.
IDSP (Integrated Disease Surveillance Program)	https://idsp.nic.in/
National Centre for Disease Control	https://ncdc.gov.in/
IDSP State Surveillance Officers	https://idsp.nic.in/inde×1.php?lang=1&level=1&sublinkid=6614&lid=4552
VRDL details for monkeypox testing	https://ncdc.gov.in/inde×4.php?lang=1&level=0&linkid=137&lid=885
Disease alerts	https://main.mohfw.gov.in/media/disease-alerts.
Monkeypox Resources	https://www.cidrap.umn.edu/monkeypox/resources.

Conflicts of interest

There are no conflicts of interest.

References

1. Magnus PV, Andersen EK, Petersen KB, Birch-Andersen A. A pox-like disease in cynomolgus monkeys. Acta Pathol Microbiol Scand 1959;46:156-76.
2. Second meeting of the International Health Regulations (2005) (IHR) Emergency Committee regarding the multi-country outbreak of monkeypox. Available from: https://www.who.int/news/item/23-07-2022-second-meeting-of-the-international-health-regulations-(2005)-(ihr)-emergency-committee-regarding-the-multi-country-outbreak-of-monkeypox. [Last accessed on 2022 Aug 12].
3. Marennikova SS, Seluhina EM, MalCeva NN, Cimiskjan KL, Macevic GR. Isolation and properties of the causal agent of a new variola-like disease (monkeypox) in man. Bull World Health Organ 1972;46:599-611.
4. Alakunle E, Moens U, Nchinda G, Okeke MI. Monkeypox virus in Nigeria: Infection biology, epidemiology, and evolution. Viruses 2020;12:1257.
5. India confirms first case of monkeypox in WHO South East Asia Region. WHO; 15 July 2022. Available from: https://www.who.int/southeastasia/news/detail/15-07-2022-india-confirms-first-case-of-monkeypox-in-who-south-east-asia-region. [Last accessed on 2022 Aug 12].
6. 2022 Monkeypox outbreak global map. CDC; 09 August 2022. Available from: https://www.cdc.gov/poxvirus/monkeypox/response/2022/world-map.html. [Last accessed on 2022 Aug 17].
7. Nine monkeypox cases in India: Six with International travel history. The Tribune; 10 August 2022. Available from: https://www.tribuneindia.com/news/nation/8-monkeypox-cases-in-india-5-with-international-travel-history-government-in-rajya-sabha-418112. [Last accessed on 2022 Aug 12].
8. India confirms first monkeypox death in Asia. Fox News Channel; 2022. Available from: https://www.foxnews.com/health/india-confirms-first-monkeypox-death-asia. [Last accessed on 2022 Aug 12]
9. 15 VRDL's for Monkeypox surveillance. Available from: https://ncdc.gov.in/inde×4.php?lang=1&level=0&linkid=137&lid=885. [Last accessed on 2022 Aug 12]
10. Guidelines for management of monkeypox disease. Ministry of Health and Family Welfare, Government of India; 2022. Available from: https://main.mohfw.gov.in/sites/default/files/Guidelines%20for%20Management%20of%20Monkeypox%20Disease.pdf. [Last accessed on 2022 Aug 12].
11. Hutchinson D, Kunasekaran M. Emergence of novel orthopox virus in Alaska, USA. Global Biosecurity 2022;4:10.
12. Deshmukh P, Vora A, Tiwaskar M, Joshi S. Monkeypox: What do we know so far? A short narrative review of literature. J Assoc Phy Ind 2022;70:11-2.
13. Luo Q, Han J. Preparedness for a monkeypox outbreak. Infect Med 2022. doi: https://doi.org/10.1016/j.imj. 2022.07.001.
14. Isidro, J, Borges, V, Pinto, M, Sobral D, Santos JD, Nunes A, *et al.* Phylogenomic characterization and signs of microevolution in the 2022 multi-country outbreak of monkeypox virus. Nat Med. 2022 Jun 24. doi: https://doi.org/10.1038/s41591-022-01907-y. Epub ahead of print. PMID: 35750157.
15. Kaler J, Hussain A, Flores G, Kheiri S, Desrosiers D. Monkeypox: A comprehensive review of transmission, pathogenesis, and manifestation. Cureus 2022;14:e26531. doi: 10.7759/cureus. 26531.
16. Weinstein RA, Nalca A, Rimoin AW, Bavari S, Whitehouse CA. Re-emergence of monkeypox: Prevalence, diagnostics, and countermeasures. Clin Infect Dis 2005;41:1765-71.
17. Sejvar JJ, Chowdary Y, Schomogyi M, Stevens J, Patel J, Karem K, *et al*. Human monkeypox infection: A family cluster in the midwestern United States. J Infect Dis 2004;190:1833-40.
18. Yinka-Ogunleye A, Aruna O, Ogoina D, Aworabhi N, Eteng W, Badaru S, *et al*. Re-emergence of human monkeypox in Nigeria, 2017. Emerg Infect Dis 2018;24:1149-51.
19. Català A, Clavo Escribano P, Riera J, Martín-Ezquerra G, Fernandez-Gonzalez P, Revelles Peñas L, *et al*. Monkeypox outbreak in Spain: Clinical and epidemiological findings in a prospective cross-sectional study of 185 cases. Br J Dermatol. 2022 Aug 2. doi: 10.1111/bjd. 21790. Epub ahead of print. PMID: 35917191.
20. Thornhill JP, Barkati S, Walmsley S, Rockstroh J, Antinori A, Harrison LB, *et al*. SHARE-net Clinical Group. Monkeypox virus infection in humans across 16 countries-April-June 2022. N Engl J Med. 2022 Jul 21. doi: 10.1056/NEJMoa2207323. Epub ahead of print. PMID: 35866746.
21. Bunge EM, Hoet B, Chen L, Lienert F, Weidenthaler H, Baer LR, *et al*. The changing epidemiology of human monkeypox—A potential threat? A systematic review. PLoS Negl Trop Dis 2022;16:e0010141. doi: 10.1371/journal.pntd. 0010141.
22. Zachary KC, Shenoy ES. Monkeypox transmission following exposure in healthcare facilities in nonendemic settings: Low

risk but limited literature. Infect Control Hosp Epidemiol 2022;43:920-4.
23. Petersen E, Kantele A, Koopmans M, Asogun D, Yinka-Ogunleye A, Ihekweazu C, *et al*. Human monkeypox: Epidemiologic and clinical characteristics, diagnosis, and prevention. Infect Dis Clin North Am 2019;33:1027-43.
24. Multi-country outbreak of monkeypox, External situation report #2-25 July 2022. WHO; 2022. Available from: https://www.who.int/publications/m/item/multi-country-outbreak-of-monkeypox--external-situation-report--2---25-july-2022. [Last accessed on 2022 Aug 12].
25. Monkeypox: Signs and symptoms. CDC; 5 August 2022. Available from: https://www.cdc.gov/poxvirus/monkeypox/symptoms.html. [Last accessed on 2022 Aug 12].
26. Harris E. What to know about monkeypox. JAMA 2022;327:2278-9.
27. Reynolds MG, McCollum AM, Nguete B, Shongo Lushima R, Petersen BW. Improving the care and treatment of monkeypox patients in low-resource set- tings: Applying evidence from contemporary biomedical and smallpox biodefense research. Viruses 2017;9:380.
28. Benites-Zapata V, Ulloque-Badaracco JR, Alarcon-Braga EA, Hernandez-Bustamante EA, Mosquera-Rojas MD, Bonilla-Aldana DK, *et al*. Clinical features, hospitalisation and deaths associated with monkeypox: A systematic review and meta-analysis. Ann Clin Microbiol Antimicrob. 2022 Aug 10;21 (1):36. doi: 10.1186/s12941-022-00527-1. PMID: 35948973; PMCID: PMC9364300.
29. Titanji BK, Tegomoh B, Nematollahi S, Konomos M, Kulkarni PA. Monkeypox: A contemporary review for healthcare professionals. Open Forum Infect Dis 2022;9:ofac310. doi: 10.1093/ofid/ofac310.
30. State Surveillance Officers. Available from: https://idsp.nic.in/index1.php?lang=1&level=1&sublinkid=6614&lid=4552. [Last accessed on 2022 Aug 12].
31. Grosenbach DW, Honeychurch K, Rose EA, Chinsangaram J, Frimm A, Maiti B, *et al*. Oral tecovirimat for the treatment of smallpox. New Engl J Med 2018;379:44-53.
32. Interim clinical guidance for the treatment of monkeypox. CDC 28 July 2022. Available from: https://www.cdc.gov/poxvirus/monkeypox/clinicians/treatment.html#anchor_165548813724. [Last accessed on 2022 Aug 12].
33. Wittek R. Vaccinia immune globulin: Current policies, preparedness, and product safety and efficacy. Int J Infect Dis 2006;10:193-201.
34. Fine PE, Jezek Z, Grab B, Dixon H. The transmission potential of monkeypox virus in human populations. Int J Epidemiol 1988;17:643-50.
35. Rao AK, Petersen BW, Whitehill F, Razeq JH, Isaacs SN, Merchlinsky MJ, *et al*. Use of JYNNEOS (Smallpox and Monkeypox Vaccine, Live, Nonreplicating) for preexposure vaccination of persons at risk for occupational exposure to orthopoxviruses: Recommendations of the Advisory Committee on Immunization Practices—United States, 2022. MMWR Morbid Mortal Wkly Rep 2022;71:734-42.
36. Sah R, Abdelaal A, Reda A, Katamesh BE, Manirambona E, Abdelmonem H, *et al*. Monkeypox and its possible sexual transmission: Where are we now with its evidence? Preprints 2022:2022070314. (doi: 10.20944/preprints202207.0314.v1).