Review article

Overview on Monkey Pox an Emerging Viral Infection. A Review of Literature

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Abstract

Aim: To reiterate the extent of problem of Monkey pox in our country and to acknowledge the problem and to implement the preventive measures as suggested by the Indian government (ICMR guidelines) by Health care professionals as well as Indian public.

Objectives: Monkey pox is a zoonotic infection caused by a virus that belongs to DNA family Poxviridae. Recently there has been upsurge in the number of monkey pox cases in our country. This has led to increase in the awareness programs in our country by WHO as well as Indian Government. Especially with strict implementation of preventive measures this viral disease can be easily preventable as happened recently with smallpox virus which belongs to same family. This review of literature is made simple for the awareness of the preventive measures suggested by WHO for health care professionals as well as general public. This DNA virus shows mutations less frequently compared to COVID -19 which has recently caused devastating Pandemic all over the world. An account on life cycle and pathogenesis is useful for further research in directing the different therapeutic modalities against the disease. Standard ICMR guidelines needed to be followed for laboratory diagnosis, treatment and prophylaxis of the suspected cases. Proper transportation of the appropriate specimens like nasopharyngeal swabs, skin lesion materials to apex laboratories through IDSP portal, in triple packing especially need proper guidelines suggested by WHO. This review can give overview on all the aforementioned aspects.

Conclusion: Monkey pox in our country is still less prevalent compared to western Africa. Proper awareness on laboratory diagnosis, treatment and preventive measures can almost all make it less significant disease in our country.

Key words: Monkeypox, DNA virus, WHO guidelines, skin lesion material, Apex laboratories, IDSP portal, triple packing, Preventive measures.

Introduction

Monkey pox virus (MPXV) is an enveloped, large, oval or brick shaped, double-stranded DNA virus with 200,000 base pairs that belongs to the Ortho poxvirus genus of the Poxviridae family [1,2,3]. Infection with any of the Ortho pox viruses provide protection against other member as the viruses are cross reactive and cross protective. [4] This provides us with a lot of insight into epidemiological preparedness. If it is included under poxviridae which includes smallpox, vaccinia, camel pox etc., the same preventive measures taken for them can be taken for monkey pox also for its prevention because of this shared antigenic nature among Ortho poxviridae group [5]. As it is an enveloped, DNA virus the targets for treatment will be envelope viral proteins and DNA polymerase and DNA viruses are stable and undergo less mutations compared to RNA viruses. Higher stability of double-stranded

DNA and the 3′–5′ proofreading exonuclease activity of poxvirus DNA polymerase is responsible for stability [6] As the virus contains 200000 base pairs genomic sequencing can be done to know further pathogenesis and virological details.

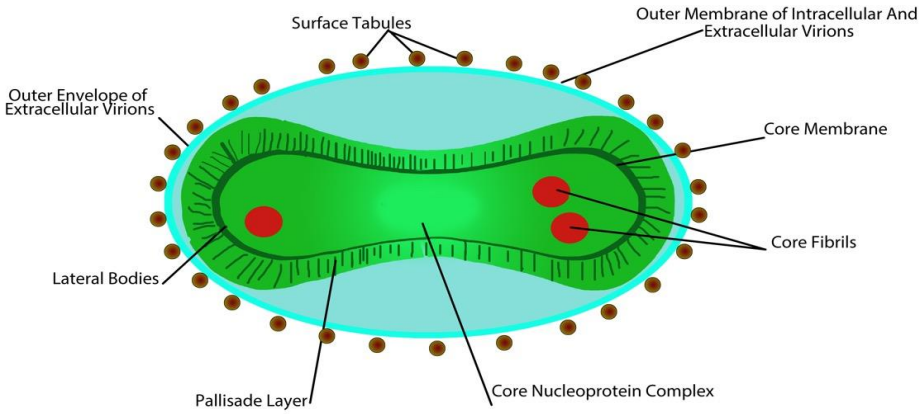


Figure 1:

Monkey pox virus is a zoonotic infection isolated in 1958 from Crab eating Macaques. The term monkey pox is a misnomer as it can also be transmitted from squirrels, rats, mice, rodents. There are two distinct genetic clades of the monkey pox virus – the Central African (Congo Basin) clade and the West African clade. The Congo Basin clade has historically caused more severe disease (10% mortality and was thought to be more transmissible. The geographical division between the two clades has so far been in Cameroon - the only country where both virus clades have been found. Natural reservoir is yet unknown. However, certain rodents (including rope squirrels, tree squirrels, Gambian pouched rats, dormice) and non-human primates are known to be naturally susceptible to monkeypox virus. [8,9,10,11,12] With the characteristic umbilicated intensely painful lesions and its high contagious nature, should we need to be worried about this emerging infectious disease? It is not massively transmitted and also will not undergo rapid mutations like Covid 19 that has recently caused massive pandemic all over the world, and has marked cross protection because of herd immunity provided by massive immunisation that were existed till recently , until the eradication of small pox in our country.

It is the causative agent of a rare emerging zoonotic infection endemic in central Africa and Western Africa even though distributed all over the world. The disease was limited to special social and sexual networks. Though its transmission through semen (virus has special predilection for testes) is also speculated, it is the skin-to-skin contact at the genital and peri genital area through vesicular fluid that the disease is majorly transmitted based on which the preventive measures can be taken. [13] As it is a stable DNA virus mutations are rare. APOBECS may be the possible reason for recent increase in the viral mutation rate by decreasing the cytosine content and increasing thymine content due to cytosine deamination [14,15,16] Similar to small pox effective vaccine can eradicate the disease. It comparatively causes milder infection than smallpox. The virus enters through mucous membrane of upper respiratory tract wherein during early phases of infection nasopharyngeal and oropharyngeal swabs can serve the purpose of diagnosis. After viral entry primary multiplication occurs in lymphoid tissue draining the site of entry. Transient primary viraemia results in infection of reticuloendothelial cells throughout the body. The virus exists in two forms 1. intracellular

mature virus and extra cellular enveloped virus. Initially primary viremia is mild there is spread of virus to regional lymph nodes such as maxillary, cervical and inguinal lymph nodes leading to lymphadenopathy [17]

Viral entry occurs through glycosaminoglycans such as chondroitin sulphate and heparan sulphate in respiratory and oral cavity [18,19,20,21] The virus undergoes complicated cell cycle inside dendritic cell, macrophages i.e., APCS followed by release of virions through cell lysis this along with cytotoxic T cell mediated skin damage that leads to appearance of skin lesions in the secondary viremia. Fever followed by appearance of macules, papules, pustule, vesicles. Secondary viraemia leads to spreading of infection to lungs, kidneys, intestines, liver, brain etc., that can lead to splenomegaly, septicaemia, secondary pneumonia, encephalitis ocular involvement can lead to blind ness [22,23,24,25,26]. During pre - eruptive phase the disease was barely infective. By 6 - 9 th day the lesions in the mouth tended to ulcerate and discharge virus Thus early in the disease the virus originated in the lesions of the mouth & URT . Later, Pustules break down and discharged the virus into the environment [27,28,29,30].

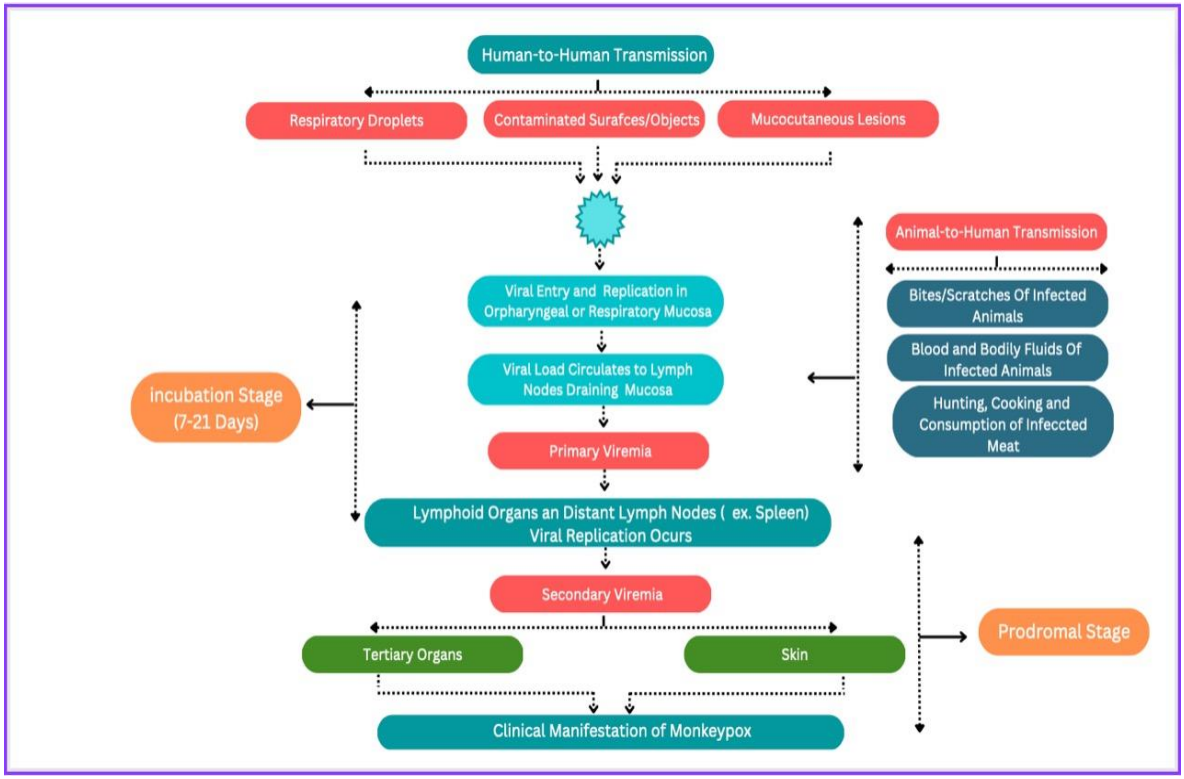


Figure 2:

Histopathological Examination of the skin showed cell proliferation & cytoplasmic inclusions of the stratum spongiosum. There was proliferation with mononuclear cells particularly around dermal vessels. Epidermal cells become swollen through distension of cytoplasm and underwent balloon degeneration with enlargement of cytoplasmic vacuoles.

The cell membrane breaks down and coalesced with neighbouring similarly affected cells resulting in the formation of vesicles. The vesicles enlarged and then become filled with white cells and tissue debris. All of the layers of the skin are involved with subsequent dermal necrosis This is responsible for scarring after infection.

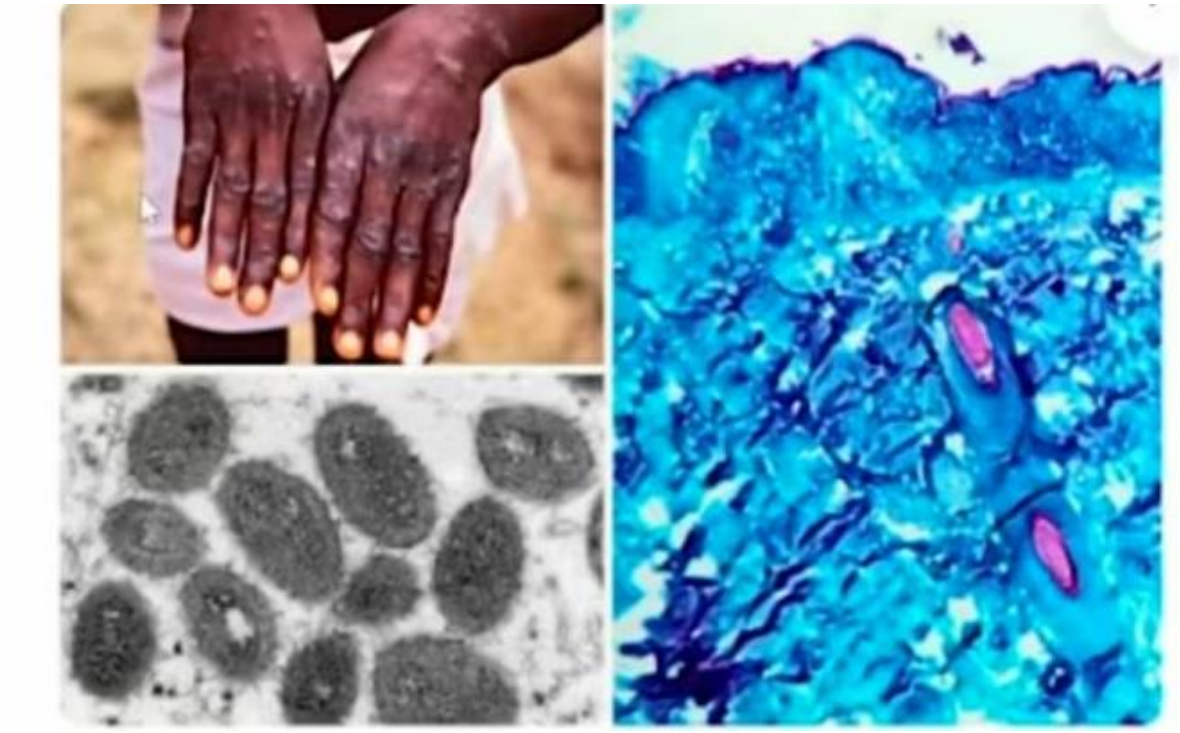
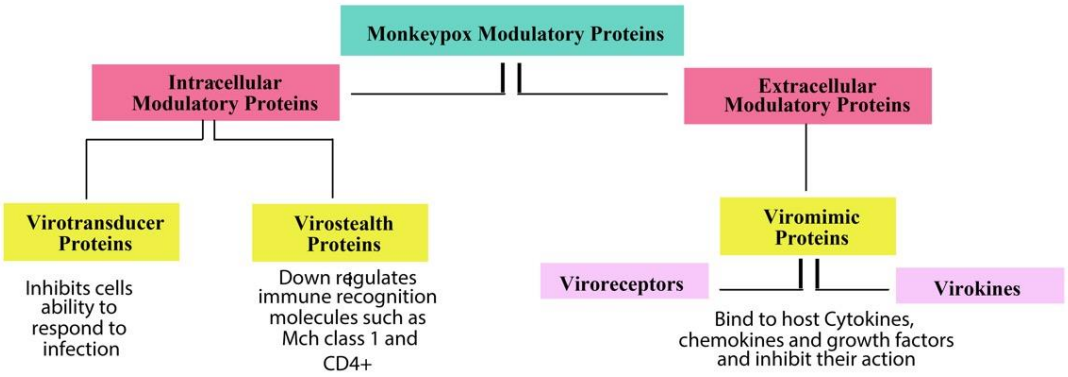


Figure 3:

Immunopathogenesis of the Monkeypox explains the reduced virulence of west African clade monkey pox. This is explained due to deletions and fragmentations in the open reading frames of its genome Another reason for reduced virulence is due to a gene that inhibits compliment enzymes (acts as immune modulator) is absent in West African clade but present in central African clade. Thereby Central African clade is more virulent than West African clade. Due to large size of the virus MPX cannot breach the host defences by passing through gap junctions and also large size of the virus leads to easy recognition of the virus to human immune system . Large size of the virus also makes it difficult for the virus to replicate rapidly (prolonged incubation period) Thus MPX is equipped with a set of molecules encoded by virulence genes that act as immunomodulators. These immunomodulators inhibit cells ability to respond to infection and down regulate immune recognition molecules such as MCH class 1 and CD4+ They bind to host Cytokines, chemokines and growth factors and inhibit their action [31,32]. The incubation period (interval from infection to onset of symptoms) of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days. Period of communicability is1-2 days before the rash to until all the scabs fall off/gets subsided. [33,34,35,36] .Transmission of monkey pox human-to-human transmission is known to occur primarily through large respiratory droplets generally requiring a prolonged close contact.



Intracellular and Extracellular Mondulatory Proteins of Monkeypox

Figure 4:

Case definition of monkey pox according to WHO is helpful for surveillance and epidemiological screening purposes. A person of any age having history of travel to affected countries within last 21 days presenting with an unexplained acute rash and one or more of the following signs or symptoms such as swollen lymph nodes, fever, headache, body aches, profound weakness can be labelled as suspected case. A person meeting the case definition for a suspected case, along with clinically compatible illness and has an epidemiological link (face-to-face exposure, including health care workers without appropriate PPE direct physical contact with skin or skin lesions, including sexual contact or contact with contaminated materials such as clothing, bedding or utensils is suggestive of a strong epidemiological link) can be defined as probable case.

A case which is laboratory confirmed for monkey pox virus (by detection of unique sequences of viral DNA either by polymerase chain reaction (PCR) and/or sequencing) can be labelled as confirmed case.[37] ICMR NIV, Pune guidelines are followed for the diagnosis of monkey pox. Initially as soon as the appropriate specimens are received in the laboratory PCR for Ortho pox genus (cow pox, buffalo pox, camel pox, monkey pox) will be done. If the PCR confirms the virus belongs to Ortho poxviridae then only conventional or Realtime PCR for monkey pox is done. Miniseq and next seq are done to identify the genomic sequence of the positive clinical samples.

Appropriate samples include skin lesion material such as swabs of lesion and /or exudate, roofs from more than one lesion or lesion crusts. Both dry swabs and swabs placed in VTM are suitable. Swabs from two lesions with similar appearance from different locations can be collected in one tube, however lesions, crusts and vesicular fluids should not be mixed in the same tube. In addition oropharyngeal swab also can be used for diagnosis. Negative swab must be interpreted with caution. (WHO guide lines)[38] All the appropriate clinical specimens should be transported to the Apex laboratory of ICMR-NIV Pune through the Integrated Disease Surveillance Programme
network of the respective district/state.

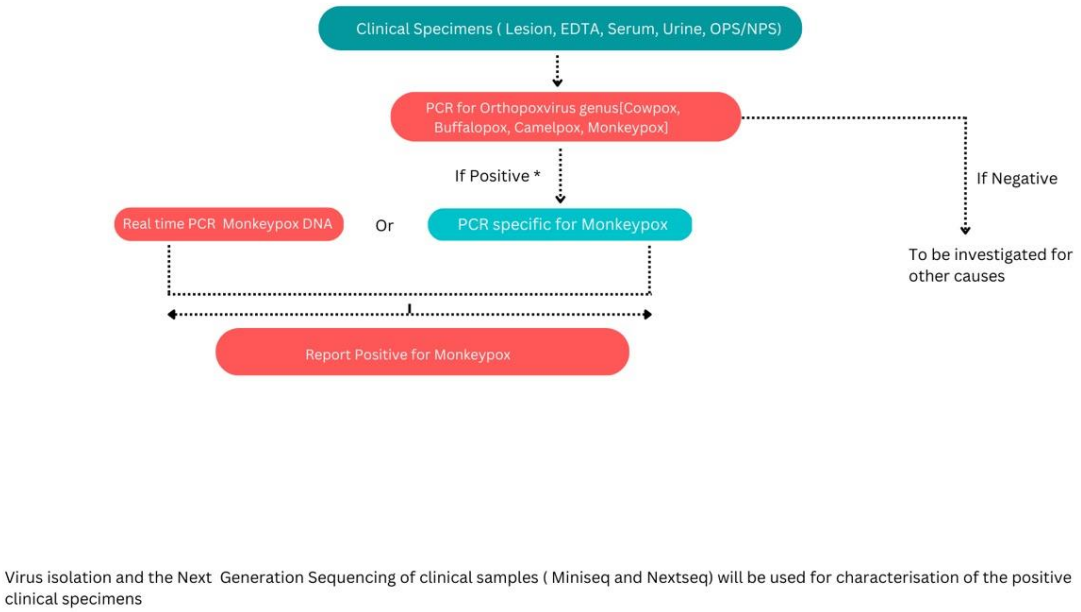


Figure 5:

Educating the people about the preventive measures and to reduce exposure to the virus are the important preventive strategies for monkey pox. Measures to be taken to prevent infection with monkeypox virus: Avoiding contact with any materials, such as bedding, that has been in contact with a sick person. Infected patients must be isolated from others. Good hand hygiene such as washing with soap and water or alcohol based sanitizers must be practiced after contact with infected animals or humans. Appropriate personal protective equipment (PPE) must be used when caring for patients to reduce risk of human-to-human transmission. Surveillance and rapid identification of new cases is precarious for outbreak containment. Close contact with infected persons is the most significant risk factor for monkeypox virus infection during human monkeypox outbreaks. Health workers and household members are at a greater risk of infection. Implementation of standard infection control precautions among HCWs can obviously reduce the infection transmission. Samples taken from people and animals with suspected monkeypox virus infection should be handled by trained staff working in suitably equipped laboratories. Patient specimens must be safely prepared for transport with triple packaging in accordance with WHO guidance for transport of infectious substances. Infection Prevention and Control (IPC) includes a combination of standard, contact, and droplet precautions that should be applied in all healthcare settings when a patient presents with fever and vesicular/pustular rash. In addition, because of the theoretical risk of airborne transmission of monkeypox virus, airborne precautions should be applied as per risk assessment. When a case has to be transported, the personnel accompanying the patient should wear PPE (long sleeved gown, N95 mask, gloves, and goggles). Prior information to the hospital of the admission/transfer of a potentially infectious person should be given. Patient has to wear a mask (if tolerated) and should follow an advice on Respiratory Hygiene and Cough Etiquette. If lesions are present, they should be covered with long sleeved clothing/pant or a clean sheet to minimize contact with others. In the ambulance disposable linen should be used if available. The ambulance should be cleaned and disinfected before using for the other patients. After wearing PPE, surfaces (stretcher, chair, door handles etc.) should be cleaned with a freshly prepared 1% hypochlorite solution or equivalent. Reusable blankets should be placed in a bag without shaking or fluffing them,

then should be kept into a laundry bag and then sent for laundering clearly labelling them so that person in the laundry wears appropriate PPE before handling or autoclaves them before opening. Manufacturer's instructions must be followed for cleaning/disinfecting reusable equipment in the ambulance. All masks and any waste contaminated with crusts, secretions, serum or body fluids should be disposed of as infectious waste in yellow bag. In the ambulance, if the driver's chamber is not separate, driver should also use PPE. Additional Precautions PPE (Disposable gown, gloves, N95 mask, Eye goggles) should be donned before entering the patient's room and used for all patient contact. All PPE should be disposed of prior to leaving the isolation room where the patient is admitted. Hand hygiene (following standard steps of hand hygiene) after all contact with an infected patient and/or their environment during care must be followed. Correct containment and disposal of contaminated waste (e.g., dressings) in accordance with Biomedical Waste Management guidelines (2016 & subsequent amendments) for infectious waste. Care when handling soiled laundry (e.g., bedding, towels, personal clothing) to avoid contact with lesion material. Soiled laundry should never be shaken or handled in manner that may disperse infectious particles. Care must be taken when handling used patient-care equipment in a manner that prevents contamination of skin and clothing. The used equipment must be cleaned and reprocessed appropriately. Provisions must be ensured for cleaning and disinfecting environmental surfaces in the patient care environment. Hospital disinfectant currently used for environmental sanitation may be used as per recommendations for concentration, contact time, and care in handling. IPC at home includes patients who do not require hospitalization thus may be managed at home taking following preventive measures: Patients should be isolated in a room or area separate from other family members. Healthy household members should limit contact with the patient. Patients should not leave the home except for medical care. No visitors should be allowed at home. Patients, especially those who have respiratory symptoms (e.g., cough, shortness of breath, sore throat) should wear a surgical mask. If this is not feasible, other household members should consider wearing a surgical mask when in the presence of the patient. Disposable gloves should be worn for direct contact with lesions and disposed of after use. Skin lesions should be covered to the best extent possible (e.g., long sleeves, long pants) to minimize risk of contact with others. Contaminated waste (such as dressings and bandages) has to be disposed in the Biomedical waste disposable bag. Waste should not be disposed in landfills or dumps. Proper hand washing with soap and water (or use of an alcohol-based hand rub) should be performed by the patient and other household members after touching lesion material, clothing, linens, or environmental surfaces that may have had contact with lesion material. Laundry (e.g., bedding, towels, clothing) may be washed with warm water and detergent; Care should be used when handling soiled laundry to avoid direct contact with contaminated material. Soiled laundry should not be shaken or otherwise handled in a manner that may disperse infectious particles. Dishes and other eating utensils should not be shared. Soiled dishes and eating utensils should be washed with warm water and dish washing soap. Contaminated surfaces should be cleaned and disinfected. Standard household cleaning/disinfectants may be used in accordance with the manufacturer's instructions. Pets and domestic animals should be excluded from the patient's environment. Duration of Isolation Procedures include affected individuals should avoid close contact with immune compromised persons and pregnant women until all crusts are gone. Isolation precautions should be continued until all lesions have resolved and a fresh layer of skin has formed. Vaccination in monkey pox is effective when compared to Covid-19 because Incubation period for monkey pox is long slowly evolving. [39]. As the disease is transmitted through travellers from endemic countries there are advisary guidelines for

international travellers such as avoiding close contact with sick people,monkeys,apes and contact with materials used by the sick people etc.,
Air port health organisation / physical health organisation should remain in a state of alert and familiarise with clinical presentation of monkey pox along with mandate thermal screening at air port, establish referal services and airport authorities shohld be informed about detection of suspected cases for the purpose of disinfection procedures.

Vaccination within 4 days of exposure the disease can be prevented. Vaccination 4-14 days of exposure reduces severity and duration of the disease. (according to CDC guidelines) In ACAM 2000 lesion development after successful vaccination is called "take" because of intracellular replication of the virus where as in Jynneos the vaccine virus does not replicate. This is associated with less side effects in Jynneos such as myopericarditis. 1 st Gen: Dry vax and vaccinia immune globulins – antibodies against vaccinia within14 days of exposure is given as post exposure prophylaxis in USA. USA is recommending Jynneos vaccine for adults aged 18 years to prevent monkey pox. [40,41,42] . In India mass immunisations are neither required nor mandatory appropriate 2nd and 3rd generation vaccines are recommended as post exposure prophylaxis in India.

At the end one should keep in mind following things to avoid monkey pox good nutrition, plenty of exercise, good water intake (hot and cold therapy, Hydro therapy), adequate sun shine, avoiding things that will suppress our immune system, getting plenty of fresh air, getting appropriate sleep, avoiding stress can rescues one from not only monkey pox but also from any kind of infectious diseases.

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