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Overview of new epidemic disease – Monkeypox

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ABSTRACT:
There is an uprising of a public health crises threatening the World with the emergence and spread of 2022 Monkeypox. The virus originates in animals and was transmitted to humans through yet known intermediary animals in Nigeria. There have been around 47,258 confirmed reported cases of 2022 Monkeypox and 48 deaths to date [17/09/2022]. The disease is transmitted to human through close contact with an infected person with lesions, body fluid, respiratory droplet and contaminated material such as bedding. The incubation period ranges from 3-17 days. The symptoms are usually fever, rash, and swollen lymph node. The disease is mild in most people but leaves the scars of lesions and rash for over a period of time. The disease fatality rate is estimated range of over 0-1% in older time and 3-6% in current condition. Diagnosis is by demonstration of the virus in the sample fluid swabbed from the rash by special molecular test. Treatment is essentially supportive and symptom suppressive. Prevention is avoid close contact with people who have a rash that look like Monkeypox and droplet precaution. The virus spread faster than its related ancestor but has lower fatality. The global impact of this new epidemic is yet uncertain.

I. INTRODUCTION:

Monkeypox is an etiological viral disease transmitted to humans from animal (Zoonotic) manifesting symptoms analogous to smallpox patient despite the fact being less severe [1]. Monkeypox virus [MPXV] occurs in the central and west Africa that has been related with 2003-04 upsurge in the United States (US), this epidemic is usually in vicinity to tropical rainforests and has been increasingly appearing in urban areas [1, 2].

Monkeypox virus [MPXV] adorn to the Orthopovirus genus of the Poxviridae family, as presented in figure 1. It is among one of the many zoonotic viruses which are isolated from various animals [3]. The vital hosts of Poxviruses are rodents, rabbits, and non-humans primate, which can intermittent be transmitted to human facilitating the phenomenon of human-to-human transmission [4]. Taxonomically, the Poxviridae family is additionally categorized into two principal families: Entomopoxvirinae and Chorodopoxvirinae. The subfamily classification is established on whether the virus will infect insects, such as Entemopovirinae, or infect vertebras, as is the instance with Chorodopoxvirinae [5]. The Chorodopoxvirinae family is additionally classified into 18 genera, as shown in figure 1. Each of the 18 genera confines of the Chorodopoxvirinae subfamily list several viruses, the majority of which are of zoonotic origin.The clinical presentation of the monkeypox virus is similar to that of smallpox [6].

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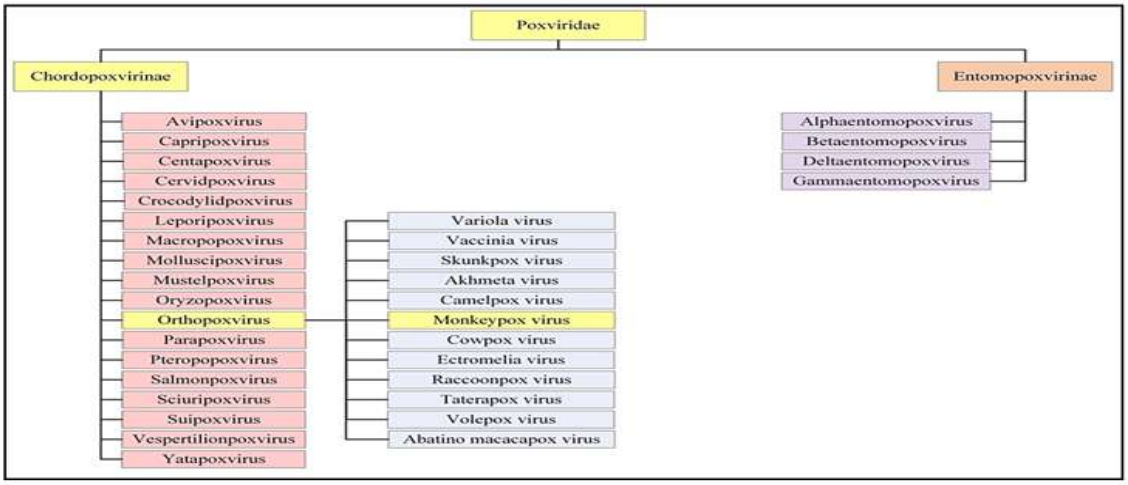

History of Monkeypox:

Monkeypox virus [MPXV] was primarily isolated and recognize in the year 1958 when monkey were shipped from Singapore to Denmark for the purpose of research got a vesicular disease [7].

Monkeypox virus[MPXV] was first reported in 1959 as an outbreak of a pox-like disease in monkeys kept at a research institute in Copenhagen, Denmark [8]. Monkeypox was first recognize in humans on 1st September 1970 in the Democratic Republic of the Congo in a 9-month-old boy in a region where smallpox had been eliminated in 1968[1]. The boy had a smallpox-like disease from which MPXV-like virus was isolated [8, 9]. It was noted to be less easily transmissible than smallpox [9]. Since 1970, human cases of monkeypox have been reported in 11 African countries: Benin, Cameroon, the Central African Republic, the Democratic Republic of the Congo, Gabon, Cote d'Ivoire, Liberia, Nigeria, and The Republic of the Congo, Sierra Leone and South Sudan with a median age of 31 years[1, 10].

From the year 1981 to 1986, over 300 cases of human-to-human transmission [11]. Small viral outbreak with death rate in the range of 10% and a secondary human-to-human infection rate of about the same amount occur routinely in Equatorial Central and West Africa[12]. In humans, the disease remained confined to the rain forests of Western and Central Africa until 2003, when an outbreak of monkeypox occurred in the U.S. All cases were traced to sick rodents imported from Ghana. Local prairie dogs caught the infection and passed it onto their owners. The disease was found to be mild and there were no deaths. [12, 13].

Between the years 1970 – 2019 the disease was reported in 10 African countries mostly in Central and West Africa [14].Monkeypox has also been reported in travelers from Nigeria to Israel in September 2018, to the United Kingdom in September 2018, December 2019, May 2021 and May 2022, to Singapore in May 2019, and to the United States of America in July and November 2021 [1]. On 31 July 2022, the first death from monkeypox was recorded in India: a 22-year-old man who had returned from the UAE died [14].

Present Condition of Monkeypox:

The initial cluster of cases were found in the United Kingdom, where the first case was detected on 6th May, 2022 in an individual with travel link to Nigeria [15]. In May 2022, numerous cases of monkeypox were identified in several non-endemic countries [1]. Since early May 2022 more than 3000 monkeypox virus infection have been reported I more than 50 countries across five region, prompting the World Health Organization [WHO] countries to declare monkeypox an "evolving threat of the moderate public health concern" on 23rd June, 2022 [16].

As of 26 August, there had been a total of 47,258 confirmed cases in over 100 countries, most of them seeing their first monkeypox cases, The United States has the highest number of monkeypox cases in the world [17].

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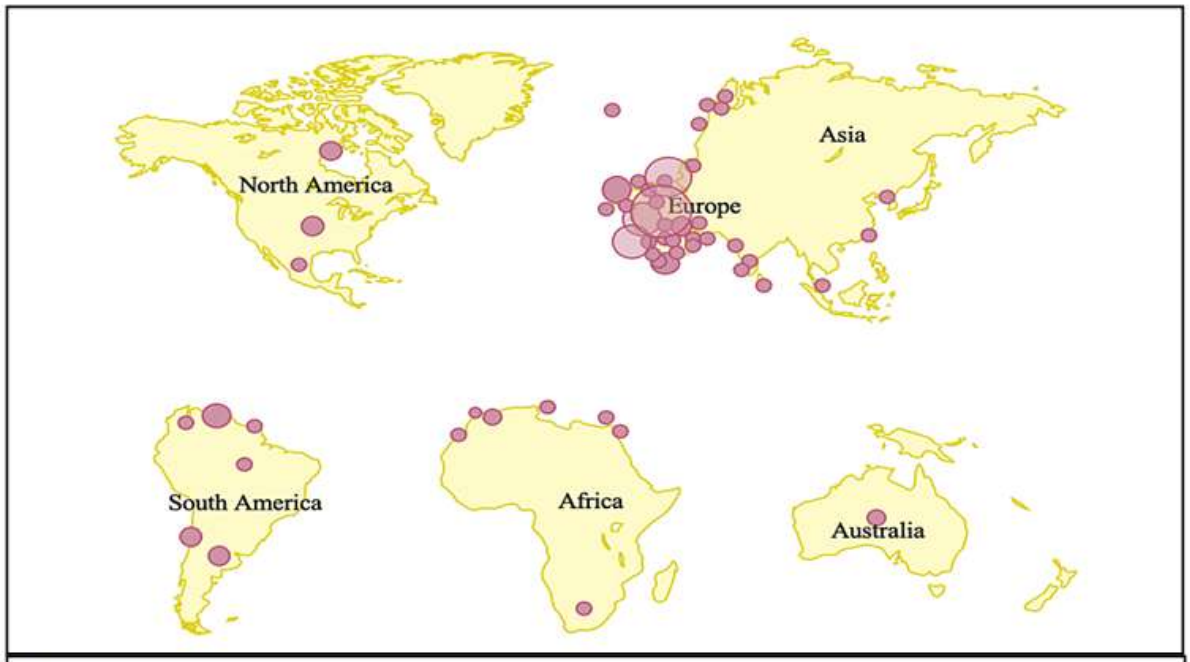

Figure 2. Showing area with affected cases of monkeypox

About Causative Agents:

Monkey pox is a virus caused by a monkey pox virus (a member of Orthopoxvirus genus in the family Poxviridae). Monkey pox is usually a self-limited disease with the symptoms lasting from 2 to 4 weeks. Severe cases can occur. In recent times, the case fatality ratio has been around 3 [18].

It is mainly spread through human contact with infected rodents; but sometimes it can also be spread through skin-to-skin contact with a person who is infected.

There are two types of monkey virus usually seen:-

1) Originated in South Africa.

2) Secondly in West Africa. Currently in 2022 it has been caused by less severe West Africa clade [19].

Monkey pox is also a viral zoonotic virus that primarily occurs in tropical rainforest areas of central and West Africa, various animal species has been found which leads to monkey pox such as Rope Squirrels, Tree Squirrels, Gambian pouched rats, Dormice, non-human primates and other species [20].

Monkey pox virus is one of the human Orthopoxvirus along with variola (VARV), Cowpox (CPX), and vaccinia (VACV). Monkey pox is similar to smallpox, but with a milder rash and lower mortality rate [21].

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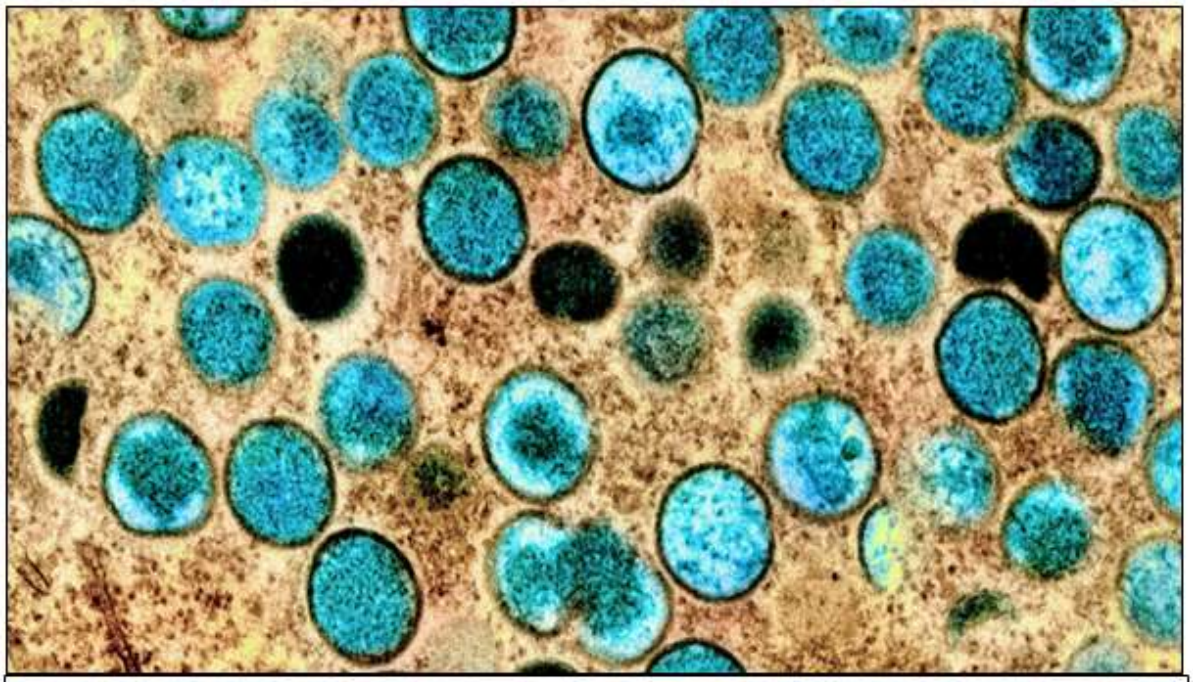

Particles found with a infected cell cultured in the laboratory.

Taxonomy of Monkeypox virus:
1) Realm: Varidaviria
2) Kingdom: Bamfordvirae
3) Phylum: Nucleocytoviricota
4) Class: Pokkesviricetes
5) Order: Chitovirales
6) Family: Poxviridae
7) Genus: Orthopoxvirus
8) Species: Monkey pox[22]

Monkey pox virus is an enveloped double-stranded DNA virus with a genome of size of around 190kb [22]. Monkey pox virus genome is about 200kb in size and encodes about 200 proteins. It is a linear double-stranded DNA genome with a covalently closed hairpin ends (no free 3' or 5' end) [23]. Although Monkey pox virus is less fatal and not as transmissible like variola virus (Causative agent of small pox), there is a concern that Monkey pox virus would become a more efficient human pathogen. So in this article, we are focusing on the viral protein that are predicted to modulate the host immune response and comparing the genome of Monkey pox virus with the genome of variola virus and vaccinia virus [24]. Some cases of Monkey pox that occurred in US revealed that respiratory transmission from an infected animal to human was possible [25]. Similarly, through respiratory droplets some human-to-human transmission occurs [26]. After infection and exposure, there is an incubation period of about 10-14 days which is then followed by period of about two days. During this period an infected person can experiences fever, chills, headache, backache, sore throat, shortness of breath and swollen lymph nodes. After this period, a maculopapular rash develop with a lesion sizes of about 0.2-1 cm [27]. This also the time when the infected person is considered the most contagious one. Lesions spread in centrifugal manner starting from face and trunk and spreading to the extremities with the involvement of palm and sole. Lesions progress through several stages during 2-4 week period going from macules to papules, vesicles, pustules [28]. In some cases, lesions results in dyspigmented scars. In some cases other manifestation such as secondary skin or soft-tissue infection, pneumonitis, ocular complications, and encephalitis have been seen [27].

Variants of Monkeypox virus:

World Health Organization (WHO) has announced new names for variants of monkey pox virus that are currently in circulation [29]. Experts in pox virology, evolutionary biology and representatives of research institutes from across the globe review the phylogeny and nomenclature

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of known and new monkey pox variants or clades [30]. They discuss the evolution and characteristics of monkey pox virus variants, their apparent phylogenetic and clinical difference, and potential consequences in public health and future virological and evolutionary research [18].

New variants by WHO such as:-

1) Former Congo Basin Clade (group of variants) in Central Africa as Clade-I, and the Former West African clade as Clade-II.

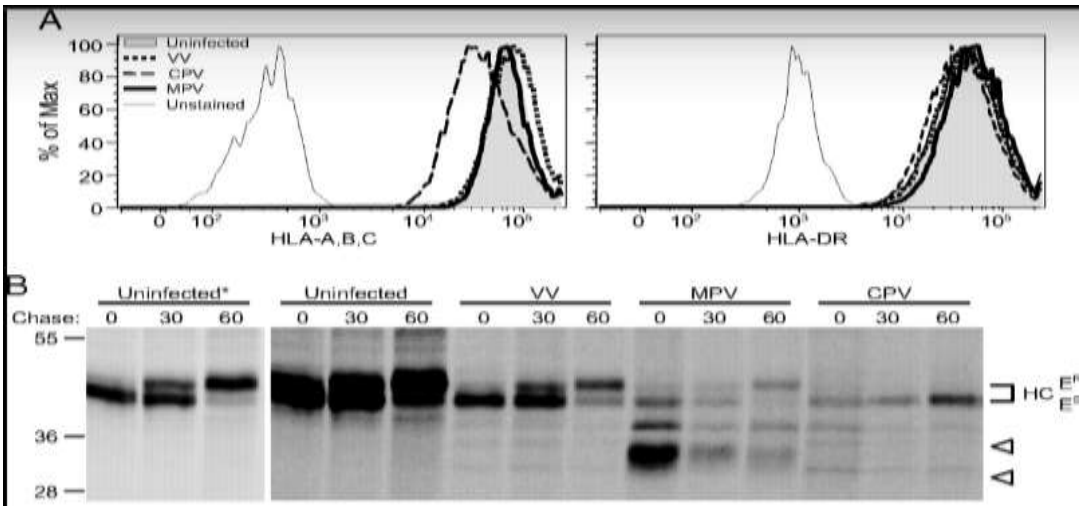
2) The later consist of two sub-clades, Clade-II-a and Clade-II-b from which Clade-II-b was the main group of variant circulating during 2022 outbreak.

3) The monkey pox virus was named when it was discovered in 1958.Major variant was identified by the geographic regions where they were known to circulate [31].

4) In 1978, Nigeria has no cases of monkey pox but from 2017 to 2022 the cases were up to 500. This was caused due to sexual contact with men [32].

Mode of attack of causative agent:

CD-14 monocytes represents the main cell type infected by these virus and they have capacity to present peptides to both virus-specific CD-4 plus and CD-8 plus T cells [33]. Monkey pox is second only to variola in terms of Orthopoxvirus virulence with mortality rate of equal to 10% [34]. The mechanism defining these form of immune invasion are not well understood. Many viruses employ a battery of immune invasion strategies [35]. We have seen that cow pox virus interfere with intracellular transport of MHC class I, the process is correlated with invasion of antiviral CD-8 plus T cell responses by cow pox virus [36]. Monkey pox encodes a close homologue of CPV-203, we expected to find similar mechanism of immune invasion by MPV. In contrast we have also seen that MPV did not down-regulate MHC class-I, but instead by using the mechanism of invasion that inhibited CD-4 plus and CD-8 plus T cell activation after cognate interactions with MPV-infected cell. This mechanism of abrogating local T cell responses may avoid systemic immune suppression, while at the same time protecting the viral reservoir from immune surveillance [37].



Risk Factors:

Dr. Lewis informed that, the people who are most exposed appear to be men who have sex with a men or others who may be in contact with them including, family members [38]. From the overall population the men who have sex with men have high chances of monkey pox. Also the people who are travelling in different countries, who may be carrying virus without knowing may also cause monkey pox virus [39].

WHO has concluded that avoid contact with sick or dead animals, as they are at high risk of monkey pox virus because of animal-to-animal transmission [39].

There are main four risk factors can be infected by monkey pox virus are as follows:-

1) Sex
2) Gender
3) Sexual Orientation

The person having multiple sex factors are at high risk of infection [40].

It has been reported that, 528 infections were diagnosed between April 27 and June 24, 2022 at 43 sites in 16 countries. Overall 98% of people were infected by bisexual men or gay, 75% were white, and 41% had immunodeficiency virus

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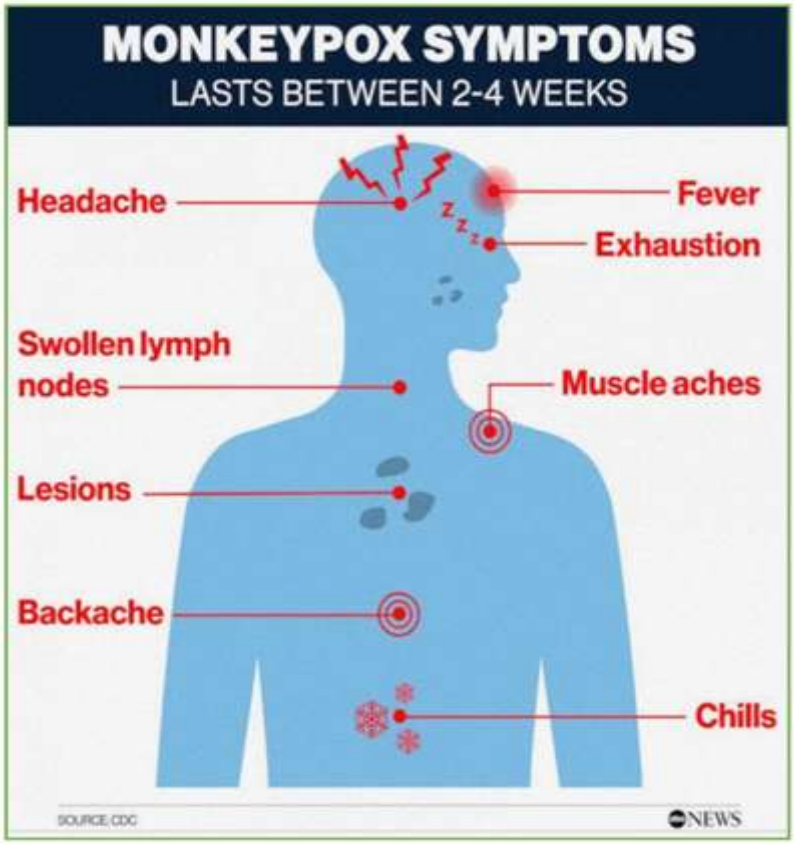
infections; the median age was 35 years. The person who is at high risk of monkey pox virus were infected the most such as 95% people were affected by sexual activity. In this case series, 95% of people were presented with a rash (with 64% having < 10 lesions), 73% had anogenital lesions, and 41% had mucosal lesions (with 54 having single genital lesions).Common systematic features preceding the rash included 62% fever, lethargy 41%, myalgia 31% and headache 27%. Lymphadenopathy was commonly reported in 56% of people. Concomitant sexually transmitted infections were reported in 29% of people who have tested. Monkey pox virus DNA was detected in 29 of the 32 person in whom seminal fluid was analyzed. Antiviral treatment was given to 5% of persons overall, and 70 (13%) were hospitalized, the reason for hospitalization was pain management, mostly for severe anorectal pain (21 persons), soft tissue super infection (18 persons), pharyngitis limiting oral intake (5 persons), acute kidney injury (2 persons), myocarditis (2 persons), and infection control purposes (13 persons). No deaths were reported [41].

Signs and symptoms:

Monkeypox is usually a self-limited disease with the symptoms lasting from 2 to 4 weeks.The incubation period of monkeypox is usually from 6 to 13 days but can range from 5 to 21 days [42].

The first symptoms of monkeypox includes:

1.A high temperature
2. A headache
3. Muscle aches
4. Backache
5. Swollen glands
6. Shivering (chills)
7. Exhaustion
8. Joint pain and Trouble breathing.
9. New or worsening chest pain.
10. Stiff neck.
11. Are confused or can't think clearly.
12. Difficulty speaking or moving.
13. Loss of consciousness.
14. Seizures [42, 43, 44, 45]



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The Infection can be divided into two periods:
A) The invasion period: lasts between 0–5 days characterized by fever, intense headache, lymphadenopathy (swelling of the lymph nodes), back pain, myalgia (muscle aches) and intense asthenia (lack of energy) [42]. Lymphadenopathy is a distinctive feature of monkeypox compared to other diseases that may initially appear similar to chickenpox, measles or smallpox [42, 43].
B)The skin eruption: usually begins within 1–3 days of appearance of fever. The rash tends to be more concentrated on the face and extremities rather than on the trunk. It affects the face (in 95% of cases), and palms of the hands and soles of the feet (in 75% of cases), along with oral mucous membranes (in 70% of cases), genitalia (30%), and conjunctivae (20%), as well as the cornea. The rash evolves sequentially from macules to papules, vesicles, pustules and crusts which dry up and fall off. The number of lesions varies from a few to several thousand. In severe cases, lesions can coalesce until large sections of skin slough off[42, 43].

Severe cases occur more commonly among children and are related to the extent of virus exposure, patient health status and nature of complications. Underlying immune deficiencies may lead to worse outcomes [44]. Complications of monkeypox can include secondary infections, bronchopneumonia, sepsis, encephalitis, and infection of the cornea with ensuing loss of vision. The extent to which asymptomatic infection may occur is unknown [43, 46].

Therapeutics:

Clinical care for monkeypox should be fully optimized to alleviate symptoms, manage complications and prevent long-term sequelae. Patients should be offered fluids and food to maintain adequate nutritional status [44, 46].Antivirals, such as tecovirimat (TPOXX), may be recommended for people who are more likely to get severely ill, like patients with weakened immune systems.First monkeypox genome from latest outbreak shows links to 2018 strain[47].The draft sequence of the virus responsible for the rapidly growing monkeypox outbreak shows it is most closely related to strains detected in the UK, Singapore and Israel in 2018 and 2019[48, 49].

There are no specific treatments available for monkeypox. Clinical management of monkeypox includes relieving symptoms and managing complications and preventing long-term

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effects [42]. Due to the genetic similarities of smallpox and monkeypox viruses, vaccines and antiviral agents used for the worldwide eradication of smallpox can also protect against monkeypox [45]. The vaccination against smallpox is approximately 85% effective in preventing monkeypox and thus prior immunization against smallpox may lead to mild disease [42].

Diagnosis:

` The diagnosis for Monkey Pox is symptomatic. The clinical differential diagnosis that must be considered includes other rash illnesses, such as chickenpox, measles, bacterial skin infections, scabies, syphilis, and medication-associated allergies. Lymphadenopathy during the prodromal stage of illness can be a clinical feature to distinguish monkeypox from chickenpox or smallpox [42, 43, 44].

If monkeypox is suspected, health workers should collect an appropriate sample and have it transported safely to a laboratory with appropriate capability as confirmation of monkeypox depends on the type and quality of the specimen and the type of laboratory test [43]. Polymerase chain reaction (PCR) is the preferred laboratory test which gives its accuracy and sensitivity [46]. For this, optimal diagnostic samples for monkeypox are from skin lesions - the roof or fluid from vesicles and pustules, and dry crusts. Where feasible, biopsy is an option. [47, 49]

In order to interpret test results, it is critical that patient information be provided with the specimens including:

A) Date of onset of fever and rash,

B) Date of specimen collection,

C) Contemporary status of the individual (stage of rash),

D) Age [50, 51]

Post monkey Pox symptoms:

Can you only get monkeypox once?

If you have already had monkeypox, you will not usually get it a second time.It is not yet known for sure whether this is also the case after vaccination. You may still develop a skin rash (including blisters) from direct skin contact with someone who has monkeypox, and those blisters are contagious [47, 48, 52].

Prevention:

Raising awareness of risk factors and educating people about the measures they can take to reduce exposure to the virus is the main prevention strategy for monkeypox. Scientific

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studies are now underway to assess the feasibility and appropriateness of vaccination for the prevention and control of monkeypox. Some countries are developing, policies to offer vaccine to persons who may be at risk such as laboratory personnel, rapid response teams and health workers.

1. Reducing the risk of zoonotic transmission.
2. Reducing the risk of human-to-human transmission.
3. Preventing monkeypox through restrictions on animal trade[42, 43, 52].

Although monkeypox is rare, there are things you can do to reduce your chance of getting it and passing it on [49].

Things you can do to avoid getting and passing on monkeypox:

Do:

1. Wash your hands with soap and water regularly or use an alcohol-based hand sanitizer.
2. Talk to sexual partners about their sexual health and any symptoms they may have.
3. Be aware of the symptoms of monkeypox if you are sexually active, especially if you have new sexual partners.
4. Take a break from sex and intimate contact if you have symptoms of monkeypox until you get seen by a doctor and told you are no longer at risk of passing it on[50, 51, 52].

Don't:

1. Do not share bedding or towels with people who may have monkeypox
2. Do not have close contact (within 1 meter) with people who may have monkeypox
3. Do not go near wild or stray animals, including animals that appear unwell or are dead, while travelling in west and central Africa
4. Do not eat or touch meat from wild animals while travelling in west and central Africa. [50, 52]

II. CONCLUSION:

This Mini-review with scientific facts was desired to make the society aware about the emerging, threatening and dreadful disease 'Monkey Pox' and the extent of the disease so far.Monkeypox infection is an important emerging pathogen that, based on serologic studies done, may result in more infections than originally believed.

If a virulent strain of monkeypox were introduced in a setting where individuals have no immunity to orthopoxviruses, this may provide the virus with the opportunity to exploit this naive population, which could lead to an epidemic and the growing lack of immunity in the population since the discontinuation of routine smallpox vaccination, has led to the concern that MPXV might be used as a bioweapon.

Our intent of this review article was to avoid any misconceptions about the disease and acknowledge the society about its severity through all the veritable information and facts.

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