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Smallpox Disease and the Novel Monkeypox Virus: A State of Knowledge at the NLS/EUS Faculty of the University of Tlemcen

Held on /06/2023, in front of the jury composed of:

President	Berrahoui S.	Lecturer class B	University of Tlemcen
Examiner	Mkedder I.	Lecturer class A	University of Tlemcen
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Dedication

To my parents

Who loved and supported me wholeheartedly throughout my life.

Who encouraged and shared with me all the emotional moments during the realization of this work.

No dedication can express my respect and love for you.

To my brothers Amine and Mounir

Your presence in my life is priceless.

You make me feel complete and unique.

I adore you.

To my family and friends

Thank you for being kind to me.

I wish you more success and happiness.

To my Tigro

Even though you're gone, you'll always be in my heart.

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I would like to thank **God** *for all the blessings, strength, and will he has given me to complete this work.*

I want to express my sincere love, respect and pride for the best and kindest human being, **Dr. Boublenza Lamia,** *Lecturer Class A at the University of Tlemcen. Thank you for all your efforts, your patience, your understanding and your encouragement that pushed me to work more and more.*

I want to express my sincere gratitude to a person with a great sense of humor, **M. Zatla Ilyes,** *PhD student at the University of Tlemcen. Really, thank you very much for all your efforts, help and valuable advice that have always been leading me to the best.*

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I would like to express my sincere respect and thanks to **Dr. Berrahoui S,** *Lecturer class B at the University of Tlemcen, for the honor that you have done me by agreeing to chair my jury*

To **all my teachers** *who believed in my abilities and encouraged me throughout my academic career.*

ملخص

بينما العالم كله مشغول ومضطرب بشأن كيفية الخروج من وباء SARS-CoV-2 بأقل ضرر ممكن، ظهر فيروس جديد ناشئ اسمه Monkeypox واستحوذ على كل الاهتمام من خلال تصدره جميع الأخبار، مع نشر الذعر بين الناس. من خلال تهديد صحتهم، وتوقع سيناريو COVID-19 في أي لحظة، إن لم يكن أسوأ.

لتقييم المعرفة حول هذا الفيروس ومرضه، ولزيادة الوعي بين أعضاء كلية العلوم الطبيعية وعلوم الحياة وعلوم الأرض والكون في جامعة تلمسان، أطلقنا استبيانًا عبر الإنترنت لمدة عشرين يومًا احتوت على أسئلة اجتماعية وديموغرافية وإدراكية حول الفيروس المستجد ومرضه والتحصين.

أظهرت النتائج التي تم الحصول عليها أن غالبية المستجيبين لدراستنا كانوا طلابًا وينتمون إلى قسم علم الأحياء. بالنظر إلى حقيقة أن الجزائر لم تسجل بعد أي حالات إصابة أو تفشي لمرض جدري القرود، فقد أثبت المشاركون مستوى معرفتهم المرضي حول هذا الفيروس المستجد ومرضه. علاوة على ذلك، أظهر معظم المشاركين موقفًا إيجابيًا تجاه اللقاح، معتبرين أنه أفضل وسيلة علاجية لمكافحة مرض MPX. على الرغم من أنMPXV قد لا يصبح وباءً، إلا أن معرفة الطرق المختلفة التي تساهم في انتشاره أمر ضروري لتجنب أي احتمال لانتشار جديد، خاصة في الجزائر.

الكلمات المفتاحية: فيروسات مستجدة، فيروس جدري القردة، مرض جدري القردة ، استبيان، جامعة تلمسان.

Abstract

While the whole world is busy about how to get out of the SARS-CoV-2 pandemic with the least possible damage, a new emerging virus named Monkeypox Virus (MPXV) appeared and captured all the attention by topping all the news, while spreading panic among people by threatening their health, expecting at any moment a COVID-19 scenario, if not worse.

To evaluate knowledge about this virus and its disease, and to raise consciousness among the members of the Faculty of Natural and Life Sciences and Earth and Universe Sciences in the University of Tlemcen, we launched an online web-based survey for a twenty days' period that contained sociodemographic and perceptiveness questions about the emergent virus, its disease, and vaccination.

Results obtained showed that the majority of the respondents of our study was students and belonged to the Department of Biology. In view of the fact that Algeria has not yet recorded any Monkeypox cases and outbreaks, the participants have proven their satisfactory level of knowledge about this emerging virus and its disease. Moreover, most participants showed a positive attitude towards the vaccine, considering it the best preventive means to fight against MPX disease.

Although the MPXV may not become a pandemic, but knowing the various ways that contribute to its spread is essential to avoid any possibility of a new, especially in Algeria.

Keywords: Emerging viruses, Monkeypox virus, Monkeypox disease, Survey, University of Tlemcen.

Résumé

Alors que le monde entier est occupé sur la façon de sortir de la pandémie de SRAS-CoV-2 avec le moins de dégâts possibles, un nouveau virus émergent nommé Monkeypox virus MPXV (La variole du singe) est apparu et a capté toute l'attention en faisant la une de toutes les nouvelles, tout en semant la panique parmi les gens, en menaçant leur santé, s'attendant à tout moment à un scénario COVID-19, sinon pire.

Afin d'évaluer les connaissances sur ce virus et sa maladie, et de sensibiliser les membres de la Faculté des Sciences Naturelles et de la Vie et des Sciences de la Terre et de l'Univers de l'Université de Tlemcen, nous avons lancé une enquête en ligne d'une durée de vingt jours qui contenait des questions sociodémographiques et de connaissance sur le virus émergent, sa maladie et la vaccination.

Les résultats obtenus ont montré que la majorité des répondants de notre étude étaient des étudiants et appartenaient au département de biologie. Compte tenu du fait que l'Algérie n'a pas encore enregistré de cas et d'épidémies de Monkeypox, les participants ont prouvé un niveau satisfaisant de connaissances sur ce virus émergent et sa maladie. De plus, la plupart des participants ont montré une attitude positive envers le vaccin, le considérant comme le meilleur moyen préventif pour lutter contre la maladie MPX.

Bien que le MPXV ne présente pas de risque de devenir, il est crucial de comprendre différentes voies à sa propagation afin de prévenir toute éventualité d'une nouvelle épidémie, notamment en Algérie.

Mots-clés : Virus émergents, Monkeypox virus, Monkeypox disease, Enquête, Université de Tlemcen.

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Chapter Three: Monkeypox Disease

Experimental Part

List of Abbreviation

AIDS: Acquired Immune Deficiency Syndrome.
APOBEC3: Apolipoprotein B mRNA-Editing Catalytic Polypeptide-like 3 enzymes.
ARDS: Severe Acute Respiratory Syndrome
CA: Central Africa.
CDC: Centers for Disease Control and Prevention.
CDV-PP: Cidofovir-diphosphate.
CHIKV: Chikungunya Virus.
CMV: Cytomegalovirus.
COVID-19: Coronavirus disease 2019.
COVs: Coronaviruses.
DENV: Dengue Virus.
DNA: Deoxyribonucleic Acid.
DRC: Democratic Republic of the Congo.
ELISA: Enzyme-linked ImmunoSorbentAssay.
EMA: European Medicines Agency.
EUS: Earth and Universe Sciences.
EVD: Ebola Virus.
EVs: Enveloped virions.
FAO: Food and Agriculture Organization.
GLEW: Global Early Warning System.
HEV: Hepatitis E Virus.
HIV: Human immunodeficiency Virus.
ICTV: International Committee on Taxonomy of Viruses.
IEVs: Intracellular Enveloped Viruses.
IFN-γ: Interferon-gamma.
IgG: Immunoglobulin G.
IgM: Immunoglobulin M.
IMVs: Intracellular Mature Virions.
ITR: Inverted Terminal Repeat.
LAMP: Loop-Mediated Isothermal Amplification.
LT4: Lymphocytes T auxiliary CD4+.
LT8: Lympogocytes T auxiliary CD8+.
MERS-CoV: Middle East Respiratory Syndrome Coronavirus.
MOPICE: Inhibitor of Complement Enzymes.
MPX: Monkeypox.
MPXV: Monkeypox Virus.
mRNA: Messenger RNA.
MVs: Mature virions.
NIV: Nipah Virus.
NLS: Natural and Life Sciences.
OIE: World Organization for Animal Health.
ORFs: Open Reading Frames.
RFLP: Restriction-Fragment-Length Polymorphism.
RNA: Ribonucleic Acid.
RPA: Recombinase Polymerase Amplification.
RT-PCR: Real-Time Reverse-Transcription Polymerase Chain Reaction.

SARS-COV: Severe Acute Respiratory Syndrome-Coronavirus.

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2.

SHD: State Health Departments.

SI: Selective Index.

SNS: Strategic National Stockpile.

SNV: Sciences de la Nature et de la Vie.

SPSS: Statistical Package for Social Sciences.

SPXV: Smallpox Virus.

STU: Sciences de la Terre et de l'Univers.

UK: United Kingdom.

UKHSA: United Kingdom Health Security Agency.

UNAIDS: United Nations Program on HIV/AIDS.

US: United Stat.

USA: United States of America.

US-FDA US: Food and Drug Administration.

VARV: Variola Virus.

VIGIV: Vaccinia Immune Globulin Intravenous.

WA: West Africa.

WHN: World Health Network.

WHO: World Health Organization.

ZIKV: Zika Virus.

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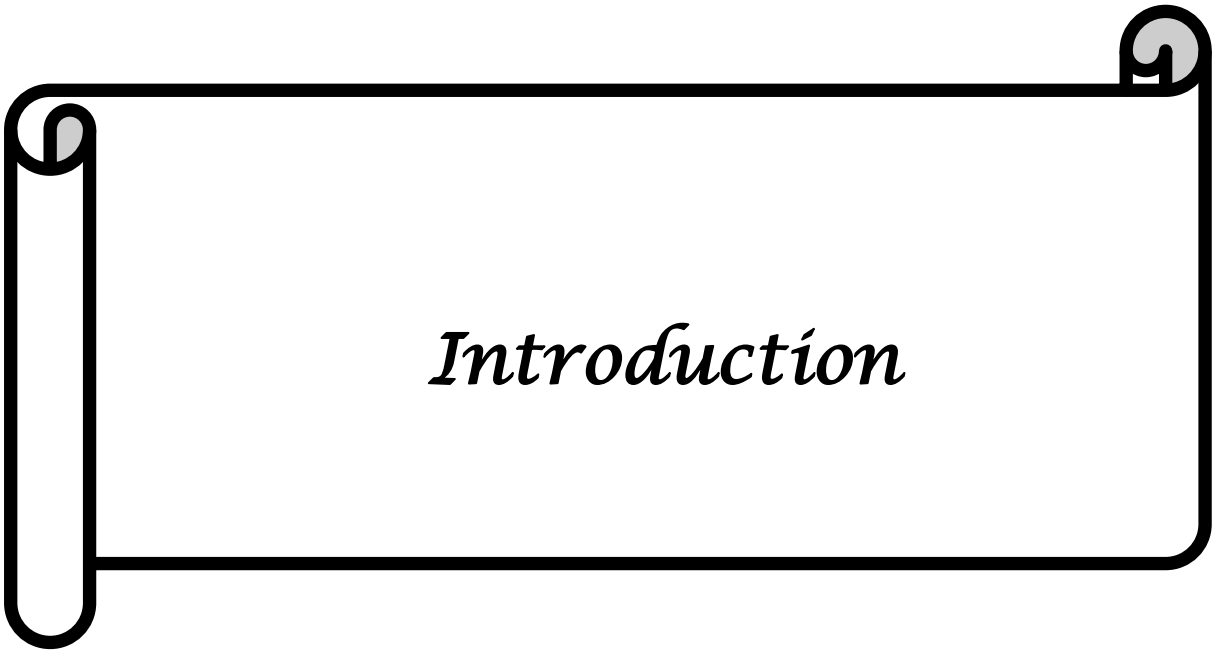

Introduction

Monkeypox virus is a zoonotic virus that belongs to the Orthopoxvirus genus **(Lansiaux *et al*., 2022),** it causes an infectious and progressive skin disease called Monkeypox which became a major public health problem in 2003 **[(Luo & Han, 2022) ; (Lu *et al*., 2022)].** Historically, this disease mainly affected the tropical rainforests of Africa, the poorest and most marginalized communities **(Luo & Han, 2022).** Due to the close contact between human populations and different components of their environment like animals, several notable viruses have suddenly emerged from obscurity or anonymity to become serious global health threats, which involve outbreaks that wreak havoc, cause panic, death, and disrupt travel and trades **[(Formenty *et al*., 2006) ; (Afrough *et al*., 2019) ; (Colón-López *et al*., 2019)].**

At a time when the world is grappling with the mutant SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) and start recovering from the negative repercussions of its pandemic, a new threat of Monkeypox virus loomed ahead **[(Abed Alah *et al.*, 2022) ; (Singhal *et al*., 2022)]**, where its first description dates back to the 1958, when it was detected in captive monkeys at the State Serum Institute in Copenhagen **(Patauner *et al*., 2022).** Since the start of this outbreak, a cumulative total of 64,290 laboratory-confirmed Monkeypox cases have been reported in 106 countries across the globe, with 20 deaths in September 21, 2022 **(Harapan *et al*., 2022).**

One of the lessons that we've learned from the COVID-19 (Coronavirus disease 2019) pandemic is to realize epidemiological investigations, understand the first few cases of outbreaks and diffuse correct information; critical points to fight and prevent them. So, through this work we wanted to evaluate the knowledge of members of the Faculty of Natural and Life Sciences and Earth and Universe Sciences (NLS/EUS) of the University of Tlemcen about the novel emergent Monekypox virus and its disease and to also spread awareness and prepare them for a possible Monkeypox virus outbreak by presenting a perception and an insight into scientific proofs of all that surrounds and involves this emerging virus and its disease.

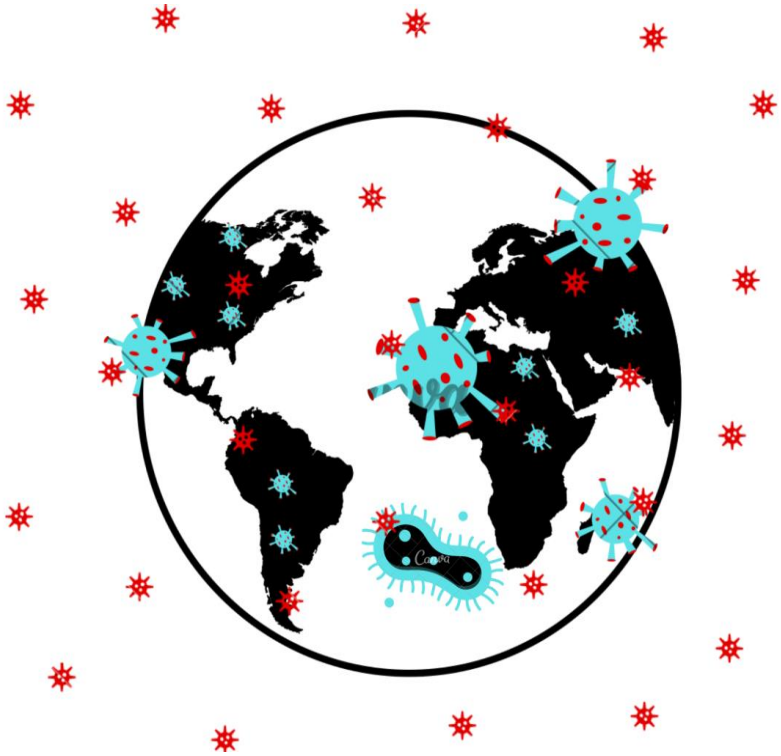
Our work was organized as a bibliographic part and a practical part, for bibliography it was divided into three chapters. Through the first chapter, we will talk about emerging viruses in general, focusing on epidemiology, the factors that favor their emergences, how it is transmitted via various routes and the best ways to prevent them. By the second chapter, we

will try to analyze the epidemiology and all characteristics of this virus including, classification, structures, genome, and its life cycle. In the third chapter, we will talk about the Monkeypox, and the possible tests used for its diagnoses, and then we will conclude this chapter with the different therapeutic approaches used to fight and prevent it like drugs and vaccines.

In the practical part, we will analyze and interpret the results that were obtained from the online created survey on Google Forms platform with anonymous responses to spread awareness and help the members of the Faculty of Natural and Life Sciences and Earth and Universe Sciences at University of Tlemcen (Teachers, Administrative-Workers and Students) to prepare for a possible Monkeypox virus outbreak in Algeria through testing their knowledge toward this emerging virus, its transmission and its disease.

Bibliographic Review

Chapter One: Emerging Human Viruses and Diseases



Emergence means the appearance of a new phenomenon within a complex system **(Choumet, 2021).** In virology, this term is used to describe viruses that appear suddenly in human populations through an animal reservoirs **(Afrough *et al*., 2019),** causing identifiable pathologies and emerging diseases that can develop into pandemics with high mortality rates **(Lina, 2005).**

Emergent viruses include three virus types; viruses that have not been previously identified (emerging), viruses that have not occurred as species before, or viruses that have appeared previously but were geographically limited (re-emerging) **(Daly, 2021).** This emergence represents one of the risks to public health and economic burdens **[(Jeong & Seong, 2017) ; (Afrough *et al*., 2019)].** Nearly, all emerging viruses have zoonotic origins **(Table 1) [(Kobayashi, 2018) ; (Diaz-Salazar & Sun, 2020)].**

Table 1:List of some Major Zoonotic Emerging Viruses (Ryu, 2017).

Family	Virus	Source of Human Infection	Reservoir Host
InfluenzaVirus	Avian InfluenzaH5N1	Chicken	Wild birds
Filovirus	Ebola virus	Primates	Bat
Flavivirus	Dengue virus	Mosquito	Monkeys
Bunyavirus	Hantaan virus	Mouse	Wild mouse
Coronavirus	SARS-CoV	Bats	Bats
Paramyxovirus	Nipah virus	Pigs	Bats
Rhabdovirus	Rabies virus	Animals (dog)	Wild animals (bats, raccoon, etc.)

1. Epidemiology of emerging viruses

The human race has survived many epidemics **(Gupta *et al*., 2021)** caused by newly emerging and reemerging viruses **(Zhao *et al*., 2017),** where a significant increase was noticed by the second half of the 20th century **(Lina, 2005).** Therefore, some examples of these emerging viruses that represent global public health concerns will be listed according to a chronological order (The year of the first isolation) **(Figure 1).**

1.1 Influenza Virus H1N1

In 1918, the world experienced the Great Influenza Pandemic, which popularly known as the Spanish Flu, and it was caused by an H1N1 virus that was identified only in 1933 **(Berbenni & Colombo, 2021)**. Hence, this disease started firstly in Europe, the United States, and some parts of Asia, after that, it spread rapidly across the world **(Golshani *et al*., 2021).** Besides, scientists classified this Spanish Flu among the most devastating pandemic in human history in terms of the overall number of victims **(Berbenni & Colombo, 2021),** which estimated to be between 50 and 100 million worldwide **(Aassve *et al*., 2021).**

1.2 Zika Virus (ZIKV)

In 1947, Zika virus was identified for the first time from the blood of rhesus monkeys in the Zika forest **(Antoniou *et al*., 2020).** After five years, it was detected in humans in Uganda and Tanzania **[(Ioos *et al*., 2014) ; (Wang *et al*., 2023 a)**]**.** ZIKV first epidemic was in the Western Pacific Ocean in 2007 **[(Singh *et al*., 2016) ; (Pierson & Diamond, 2018)].** Ahead of February 1st, 2016, the World Health Organization (WHO) declared it a Public Health Emergency of International Concern because of its rapid pandemic potential and impact on humans **(Ali *et al*., 2022).** Moreover, 52 American countries or territories reported more than 220.000 confirmed and 580.000 suspected cases in 2017 **(Pierson & Diamond, 2018).**

1.3 Chikungunya Virus (CHIKV)

Between 1952 and 1953, the Chikungunya virus was isolated for the first time in Tanzania from a febrile patient **[(Battisti *et al*., 2021) ; (Manzoor *et al*., 2022)].** In the following years, it has spread to more than 60 countries worldwide **(Kovacikova & van Hemert, 2020).** As well as, between 2005 and 2006, La Reunion Islands in the Indian Ocean mounted the appearance of the most remarkable CHIKV epidemic with statistical figures equal to 260,000 infection cases with an average of 40,000 new cases per week and 284 deaths **(Constant *et al*., 2021).**

1.4 Monkeypox Virus (MPXV)

In 1958, a Danish laboratory detected for the first time a new zoonotic virus that was named Monkeypox virus **(Mohapatra *et al*., 2022)**. Two years later, its first human-infected case was reported in the Democratic Republic of the Congo (DRC), and since then, this emerging virus spread to neighboring countries **(Wang *et al*., 2023b).** Consequently, on January, 20,2023, the WHO reported 84.916 cases and 81 deaths across 110 countries **(Mohamed *et al*., 2023).** Remarkably, from the abolition of the Variola Virus (VARV) to

date, MPXV represents the most virulent *Orthopoxvirus* threatening human public health **(Li *et al*., 2022).**

1.5 Ebola Virus (EVD)

The DRC marked the appearance of a dangerous outbreak caused by a new emerging pathogen in 1970 named the Ebola virus **[(Jacob *et al*., 2020) ; (Bisimwa *et al*., 2022)],** which resulted in the infection of 300 people and a mortality rate of 88% in Zaire and 53% in Sudan **(Chakrabartty *et al*., 2022).** After that year, EVD reported 39 outbreaks that occurred across the entire equatorial belt of Africa **(Tian *et al*., 2022).** In addition to that, the virus caused a contagious outbreak with 3470 cases and 2280 deaths in 2020 **(Frimpong & Paintsil, 2023).**

1.6 Human immunodeficiency Virus (HIV)

HIV was believed to have entered the human population through cross-species transmission from non-human primates in the 1900s' of Africa **[(McCutchan, 2006) ; (Deeks *et al*., 2015)].** However, it attacked attention in 1980s when homosexual men in urban centers began presenting with advanced and unexplained immunodeficiency due to this virus which cause a very dangerous disease called AIDS (Acquired Immune Deficiency Syndrome) **(Deeks *et al*., 2015),** and since that, it was be one of the most serious public health threats in the 21st century **(Peeters *et al*., 2013)** due to its global progress. Joint United Nations Program on HIV/AIDS (UNAIDS) estimated that there are 38 million people living with HIV worldwide **(Giovanetti *et al*., 2020).**

1.7 Nipah Virus (NIV)

In 1998, the world witnessed the first identification of a new emerging zoonotic Paramyxovirus called Nipah virus in Malaysia **(Hauser *et al*., 2021).** Afterwards, in 2001 Siliguri suffered from a large outbreak, leading to 66 probable cases and 45 deaths where the causative agent was NIV **(Aditi & Shariff, 2019).** Its latest outbreak was in Kerala, India, in 2018 which resulted in 17 deaths **(Sharma *et al*., 2019),** and in the same year, the WHO listed it as a priority disease posing a public health risk **(Sun *et al*., 2018).**

1.8 Coronaviruses (COVs)

Before 2019, the world knew six stains of coronaviruses, that infect humans and caused respiratory diseases **(Hasöksüz *et al.*, 2020),** including the Severe Acute Respiratory Syndrome-Coronavirus (SARS-COV) outbreak that occurred between November 2002 and July 2003 which caused 2465 confirmed cases worldwide and 896 fatalities and its severity circulation still exists to date **(Zatla *et al.*, 2021a),** and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) that was detected for the first time in Saudi Arabia in 2012 **(Killerby *et al.*, 2020).**

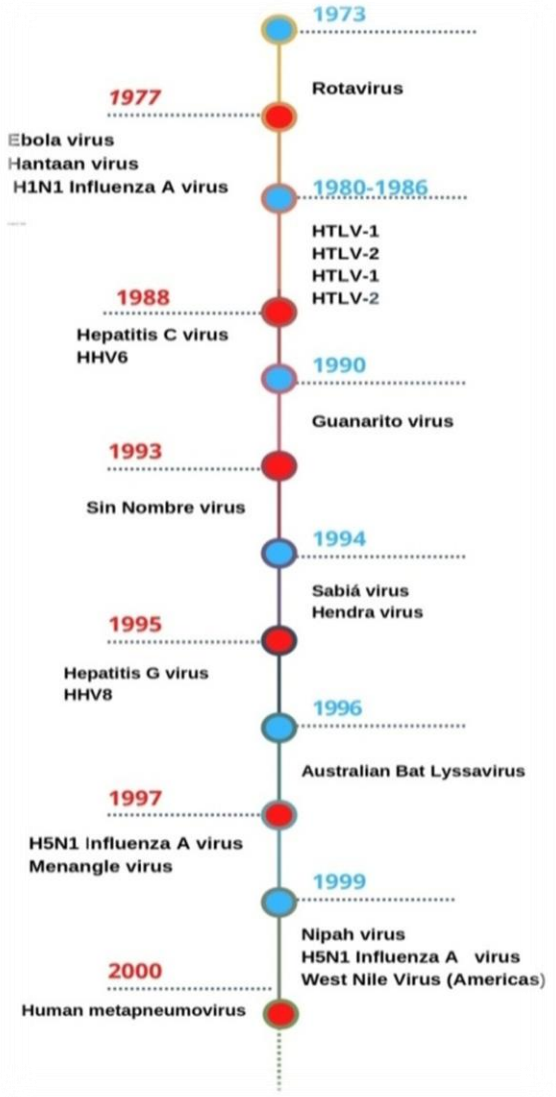


Figure 1: Timeline of emergent viruses between 1970 and 2000 (Lina, 2005).

By the end of 2019, severe respiratory infections etiologies invaded the Wuhan city, China, and signed a significant number of people **(Wu *et al.*, 2020).** Whereas**,** on February 11, 2020, The International Committee on Taxonomy of Viruses (ICTV) named this causative agent was named as SARS-CoV-2 **[(Ali & Alharbi, 2020) ; (Akram & Mannan, 2020).** By October 2022 , 232,622 cases were reported in the United Stat (US) **(Zhao *et al.*, 2022).**

2. Viral emergence and transmission

We live in a dangerous world, in which at any time, an emerging, lethal, and highly transmissible pathogens can appear **[(Lina, 2005) ; (Fischer *et al.*, 2020)].** To be able to stand against this pathogens and conquer their consequences, it would be very important to

understand the factors and transmission modes that promote their appearance and spread **(Liang *et al*., 2015).**

According to the Institute of Medicine of the National Academy of Sciences in the United States of America (USA), thirteen factors contribute to the emergence of new infectious agents and diseases **(Lina, 2005),** which can be summarized in three majors factors:

2.1 Natural evolution of viruses

Most emerging viruses possess RNA (Ribonucleic Acid) genomes **[(Holmes, 2009) ; (Choumet, 2021)],** which mutate faster than DNA (Deoxyribonucleic Acid) viruses **(Sanjuán & Domingo-Calap, 2016)** due to their short generation times **(Parrish *et al*., 2008),** resulting in errors made by RNA-dependent RNA polymerase enzymes during replication **(Lina, 2005).** Likewise, Recombination consists of establishing genetic changes with other human pathogens **(Desenclos & De Valk, 2005)** which is more common in positive-sense RNA **(Holmes & Drummond, 2007)** and segmented RNA viruses (**Dufour, 2017).** However, this phenomenon is rare in pathogens with negative-sense RNA because of the constant presence of a protective capsid around its genome **(Holmes & Drummond, 2007).**

2.2 Change in human behavioral and social status

Humans are the first responsible agent of emerging viruses appearance and spread **(Lina, 2005)** through their behaviors and habits such as sexual contacts, intravenous drug use **(Parrish *et al*., 2008) ,** and consumption of raw or undercooked food like sausages made from porcine livers which promote the transmission of Hepatitis E virus (HEV) **[(Desenclos & De Valk, 2005)].** To date, contaminated foods and water allows the transmission of pathogens like the Poliovirus, which caused many outbreaks resulting to their presence in unpasteurized raw milk **(Mattison *et al*., 2009).**

Hence, demographic pressure that leads to migration to new territories **(Choumet, 2021),** and towns that suffer from a lack of health and collective facilities favored emergence and spread of many pathogen agents like the Dengue Virus (DENV) **(Desenclos & De Valk, 2005).** Subsequently, increase in the volume of international trade and transport over the past thirty years **[(Grubaugh *et al*., 2018) ; (Zientara *et al*., 2020)].** Moreover, other factors play a significant role in viral diseases transmission such immunosuppressant, nutritional state, herd immunity, introducing of new medical interventions, limited health resources because of the lack of political commitment of countries, low education levels, war and famine **[(Burrell *et al*., 2017) ; (Malvy *et al*., 2019)].** Additionally, the immunity and physiological changes

during pregnancy, obesity and chronic diseases also allow the transmission of several diseases **[(Jamieson *et al*., 2006) ; (Martirosyan, 2020) ; (Amin *et al*., 2021)].**

2.3 Environmental changes

Climate change and global warming modify the geographical distribution of vectors which transmit virus **[(Dufour, 2017) ; (Choumet, 2021)],** such as *Aedes albopictus* (mosquito) which transmits numerous arboviruses like dengue fever and Chikungunya virus which left their habitat and migrate to the south of France **(Zientara *et al*., 2020).** Remarkably, Rainforest development increases contact between wild animals and humans, as a result, the transmission of infectious pathogens from their original hosts to new human hosts **(Ryu, 2017).** Without forgetting, deforestation also promotes the appearance and spread of emerging viruses and diseases as Ebola virus **[(Lina, 2005) ; (Parrish *et al*., 2008) ; (Gessain, 2013)].**

3. Prevention and vaccination

To prevent emerging viruses and diseases, it is high time to focus on basic strategies, investing in new diagnostic technologies **(Ellwanger *et al*., 2019).** And it is very important to share data, and make collaboration among the organization, academia, government, and companies. WHO has created a Global Early Warning System (GLEWS) in collaboration with World Organization for Animal Health (OIE) and the Food and Agriculture Organization (FAO), which aim to provide geographical spread, the early warning and risk assessment of zoonotic and emerging viruses and diseases **(Trovato *et al*., 2020).** On the other hand, it is very important to understand the mechanisms, factors, and geographic distribution of these pathogens through the development of epidemiological surveillance and investigation systems **[(Dufour, 2017) ; (Jaijyan *et al*., 2018) ; (Sun *et al*., 2018)].**

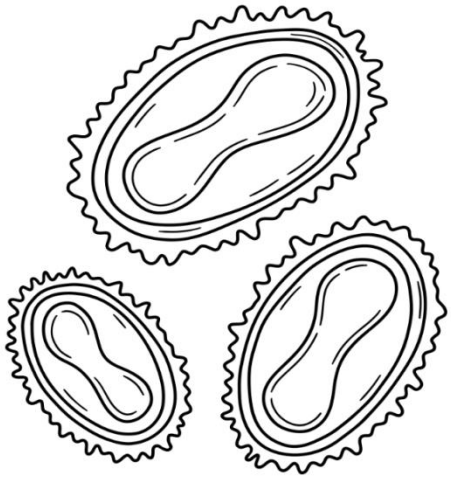
Also, to fight emerging virus, diseases and managing biodiversity it is necessary to monitor environment health by checking deforestation and sustainable land which use for managing biodiversity (**Devnath & Masud, 2021).**

To date, vaccines are the most effective method to prevent and fight emerging viruses and diseases **[(Shyr *et al*., 2021) ; (Daly, 2021)]** since Edward Jenner discovered vaccination in 1769, when he detected the possibility to vaccinate against Smallpox **(Tournier, 2019).** Sadly**,** The different nature of emerging virus, limited resources, the long time to develop and test vaccines, high need for financial resources, and manufacturing problems cause the lack of vaccines for most emerging viruses **[(Ippolito & Rezza, 2017) ; (Trovato *et al*., 2020) ;**

(Daly, 2021)]. Even if they exist, they would not be available for everyone **(Meyding-Lamadé *et al*., 2019).** So, in order to develop these vaccines, it's very important to identify the pathogen agent, analyze the viral genome, the structures and the functions of viral proteins like the specific epitopes before the outbreak events **[(Bayry, 2013) ; (Grubaugh *et al*., 2018) ; (Sun *et al*., 2018) ; (Jaijyan *et al*., 2018) ; (Ellwanger *et al*., 2019) ; (Trovato *et al*., 2020)].**

It is important to note that disinfectants and antiseptics play a significant role in fighting emerging viruses that persist on a surface and can be transfer directly to susceptible individuals **(Eggers *et al*., 2021).** Without forgetting the immune system, which combats emerging viruses and diseases, we must boost it by using functional food and bioactive compounds such as Zinc **(Martirosyan, 2020).** Besides, the access of population and healthcare worker's to education, social media and health services allow knowledge of emerging viruses transmission mode **[(Ippolito & Rezza, 2017) ; (Ellwanger *et al*., 2019)].**

Chapter Two: Monkeypox Virus



After more than two years of substantive global economic and healthcare impact of COVID-19, unfortunately, we will likely be facing a second new viral outbreak the causative agent is the Monkeypox virus **(Kumar *et al*., 2022).** Notably, MPXV is resistant to ether and drying, while easily inactivated by chloroform, methanol, formalin, and heating at 56°C for 30 minutes **(Luo & Han, 2022).**

1. Epidemiology of Monkeypox Virus

Monkeypox Virus was isolated for the first time in 1958, after a non-fatal rash disease in a burst in laboratory of monkeys at State's Serum Institutes in Copenhagen, Denmark **[(Srivastava & Srivastava, 2022) ; (Kaler *et al*., 2022) ; (de la Calle-Prieto *et al*., 2023)].** In 1970, the first human MPXV infection case was detected in a nine-month-old baby boy that has not been vaccinated against Smallpox Virus (SPXV) in Bokenda, a remote village in the Equatorial province of the DRC **[(Sklenovská & Van Ranst, 2018) ; (Ranganath *et al*., 2022) ; (Tiwari *et al*., 2023)].** In the same year, six human cases were reported from the DRC, Liberia and Sierra Leone **(Farasani, 2022).** Since the first decade (between 1970 and 1981), MPXV virus was endemic in the DRC and had spread to other African countries**,** mainly in Central and West Africa causing more than 400 confirmed cases back at the time **[(Li *et al*., 2006) ; (Farasani, 2022) ; (Bunge *et al*., 2022)].** More precisely, the first six years were characterized by the spread of these emerging pathogens in six countries with 48 documented cases, 38 cases in the DRC, 4 in Liberia, 3 in Nigeria and only one case in Cameroon, Côte d'Ivoire, and Sierra Leone **[(Gong *et al*., 2022) ; (Kumar *et al*., 2022)].**

Moreover, between 1981 and 1986, in Africa, this Smallpox still spread reaching 3838 cases and 33 deaths **(Ejaz *et al*., 2022).** Subsequently, by 1986, these cases had estimated to be more than 400 cases with mortality rates approaching to 10% **(Kumar *et al*., 2022).** After 1986, this infection began to slow down gradually, and between 1993 and 1995, it disappeared completely **(Gong *et al*., 2022).** Unfortunately, this decline did not last long, because 511 cases had reported in an outbreak in the Lodja and Katako–Kombe health zones of the DRC, between 1996 and 1997 **(Ejaz *et al*., 2022).**

The first human Monkeypox outbreak outside of Africa was in 2003 in the USA with 47 infected cases, after an infected Gambian rats transmitted the virus to humans **[(Li *et al*., 2022) ; (Fatima & Mandava, 2022) ; (Bryer *et al*., 2022)].** Then**,** from 2005 to 2007, 760 infected individuals were confirmed in the most significant forest coverage zones in the DRC, another major outbreak of 587 cases was occurred between 2014 and 2016 **(Ejaz *et al*., 2022).**

Recently, this emerging virus drew attention again (**Patauner *et al.*, 2022)** after confirmation of the first human Monkeypox virus case in a traveler returning from Nigeria by the United Kingdom Health Security Agency (UKHSA) on May 7, 2022, and since it appearance in non-African countries, including Americas, Eastern Mediterranean, European and Western Pacific regions **[(Puccioni-Sohler *et al.*, 2022) ; (Lansiaux *et al.*, 2022) ; (Nuzzo *et al.*, 2022)]** which more than over 17,300 confirmed and suspected cases were identified**,** and over 40.000 infected people in 87 countries were not MPXV endemic, like the United Kingdom (UK), Australia, Belgium, Canada, France, Germany, Italy, the Netherlands, Portugal, Spain, Sweden, and the USA **[(Gomez-Garberi *et al.*, 2022) ; (Hraib *et al.*, 2022)].**

Hence, on June 2, 2022, MPXV caused 780 infected cases in others 27 non-endemic countries **(Johri *et al.*, 2022)** and in the next day, The WHO announced this virus as an emerging risk of moderate public health concern. On June 22, 2022, the World Health Network (WHN) declared the current Monkeypox outbreak a pandemic after confirming 3,417 Monkeypox cases across 58 countries and rapidly expanding across multiple continents **(Srivastava & Srivastava, 2022).**

Resulting in many events, the WHO re-announced this dangerous virus and as a Public Health Emergency of International Concern, in July 23 **[(Nuzzo *et al.*, 2022) ; (Okyere & Ackora-Prah, 2023)].** In October 21, 2022, 75.348 confirmed cases were reported in 109 countries worldwide **(Ortiz-Saavedra *et al.*, 2022),** and by December 2022, this number increased to 83.497 laboratory-confirmed cases, 1.694 probable cases, and 72 deaths in 110 countries **(Abu-Hammad *et al.*, 2023).**

2. Monkeypox Virus

2.1 Classification

PXV belongs to Orthopoxvirus genus, and the family of Poxviridae **(Figure 2) [(Gong *et al.*, 2022) ; (Huang *et al.*, 2022) ; (Luo & Han, 2022) ; (Mileto *et al.*, 2022) ; (Ophinni *et al.*, 2022) ; (Samaranayake & Anil, 2022)].**

Additionally, comparative analysis shows that MPXV has more than 90% nucleotides (around 196.858 base pairs) and 60 amino acid residues similar to other *Orthopoxvirus* **[(Lu *et al*., 2022) ; (Tiecco *et al*., 2022)].** Phylogenetically, the genome of MPXV and VARV share a high level of sequences similarity (96.6%) and according to this level, it suggests that they did not evolve from one another **[(Huang *et al*., 2022) ; (Kmiec & Kirchhoff, 2022)].**

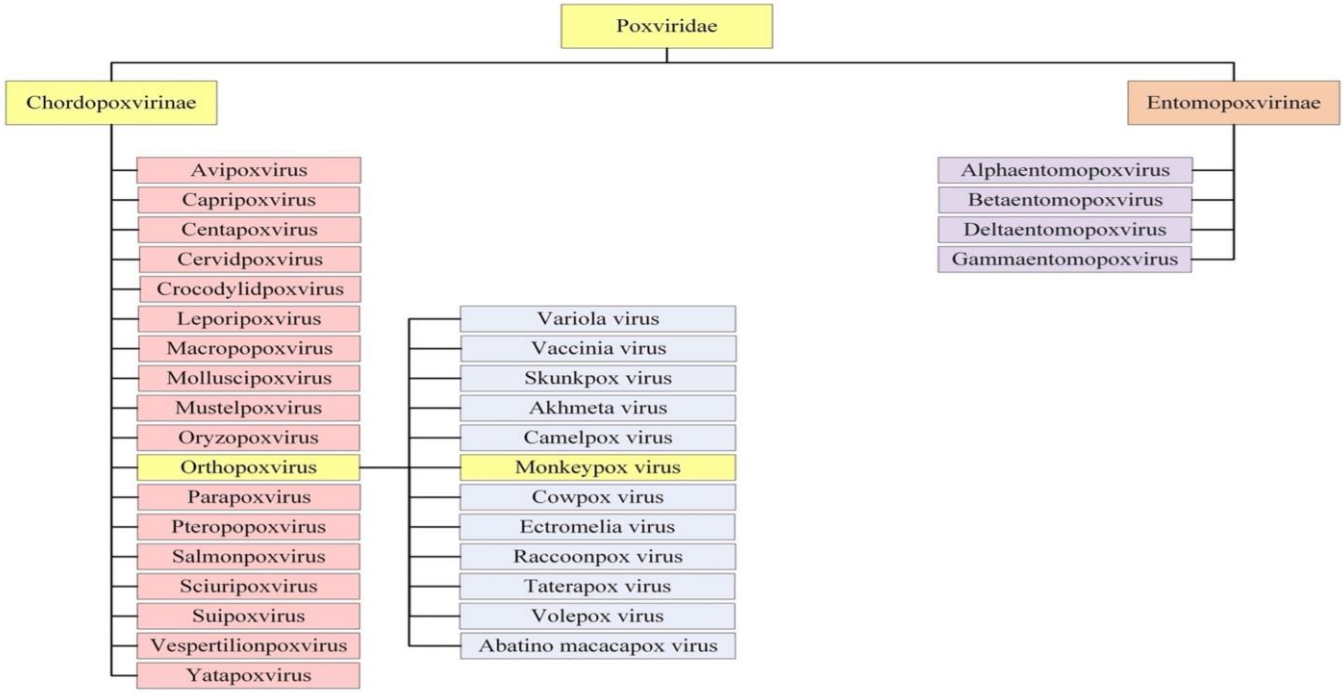


Figure 2: Taxonomy and Classification of Monkeypox within Poxviridae Lineage (Kaler *et al*., 2022).

2.2 Origin and animal's reservoir

MPXV can infect a wide range of animals like birds, reptiles, insects, mammals, which play intermediate hosts role in the natural zoonotic cycle **[(Sklenovská & Van Ranst, 2018) ; (Atkinson *et al*., 2022) ; (Di Gennaro *et al*., 2022) ; (Titanji *et al*., 2022)]** but its natural reservoir is still unknown **[(Kaler *et al*., 2022) ; (Mileto *et al*., 2022)].** Till now, this virus has been isolated from wild animals only twice: in 1985 in DRC in a rope squirrel (*Funisciurus anerythrus*), and in sooty mangabey (*Cercocebus atys*) in Ivory Coastin in 2012, so scientists suggest that these species may be the original reservoir of this emerging virus **[(Sklenovská & Van Ranst, 2018) ; (Ejaz *et al*., 2022) ; (Mileto *et al*., 2022) ; (Xiang & White, 2022)].**

2.3 Structure

Monkeypox virus has two distinct infectious forms, extracellular Enveloped Virions (EVs) and intracellular Mature Virions (MVs) **(Figure 03) [(Alakunle *et al*., 2020) ; (Gong**

***et al*., 2022) ; (Lansiaux *et al*., 2022) ; (Lum*et al*., 2022)].** Electron microscopy of MV shows an ovoid or brick-shaped particle measuring between 200 and 250 nm, surrounded by a 30 nm lipoprotein outer membrane with a tubules or filaments surface. As well, it has a large double-stranded linear DNA genome with a double concave dumbbell-shaped nucleoprotein. In addition to an envelope, the mature EV represents the same constructions as that of MV **[(Harapan *et al*., 2022) ; (Li *et al*., 2022) ; (Upadhayay *et al*., 2022) ; (Zhu *et al*., 2022) ; (Ejaz *et al*., 2022) ; (Farasani, 2022) ; (Li *et al*., 2023) ; (Sepehrinezhad *et al*., 2023) ; (Mitjà *et al*., 2023)].**

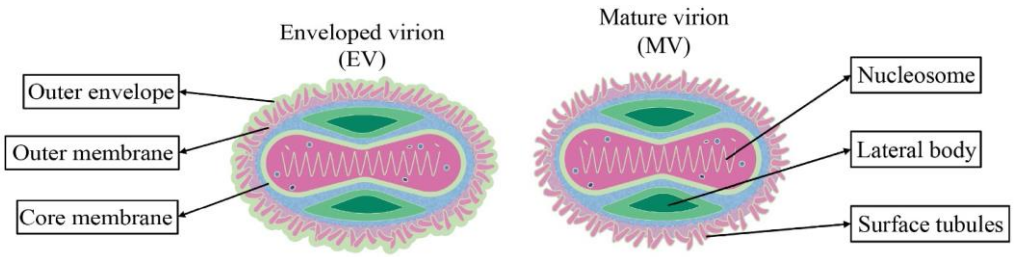


Figure 3 : Structure of the two Monkeypox viruses forms (EV and MV) (Zhu *et al*., 2022).

2.4 Genome

MPXV genome is a linear double-stranded DNA measuring about 197 kb with more than 190 non-overlapping Open Reading Frames (ORFs) that each one formed by more than 60 amino acid residues long **[(Gong *et al*., 2022) ; (Harapan *et al*., 2022) ; (Hraib *et al*., 2022) ; (Ophinni *et al*., 2022)].** This large genome has bipartite covalently closed which contains an identical but oppositely oriented 6379 bp Inverted Terminal Repeat (ITR) sequence at the end of the genome **(Zhu *et al*., 2022).**

The genes of this virus can be divided into two types, conserving geneses which encode all the proteins needed for viral infectious cycle, and the non-conserved genes which are mostly associated with the immune escape of the poxvirus **(Figure 4) [(Gong *et al*., 2022) ; (Mitjà *et al*., 2023)].**

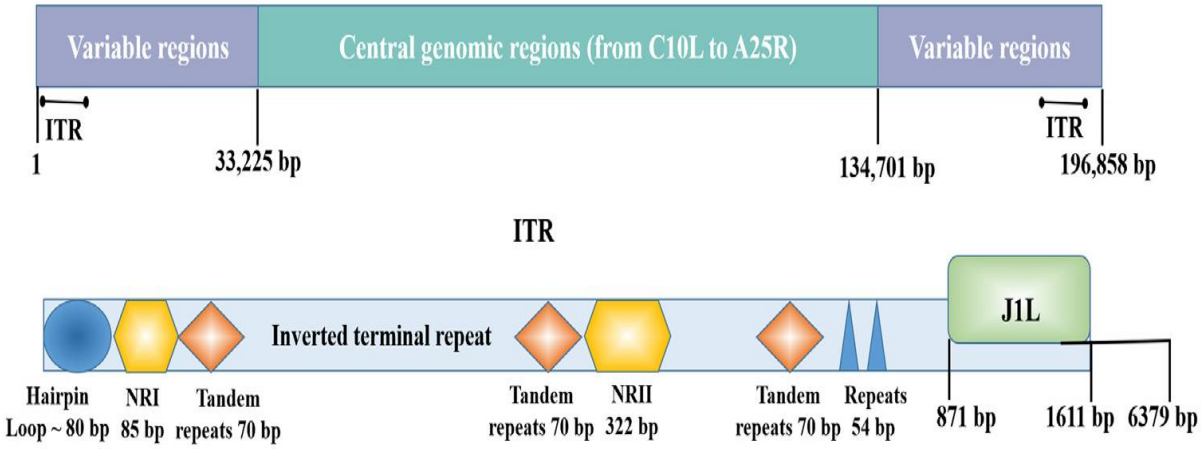


Figure 4: Genome of Monkeypox virus (MPXV) (Li *et al*., 2023).

2.5 Mutations

Monkeypox virus does not present a lot of mutations compared to RNA viruses due to the high stability of their genome and the 3'-5' correction activity of poxvirus exonuclease **[(Huang *et al*., 2022) ; (Kmiec & Kirchhoff, 2022)].** Scientists suggest that these mutations may be caused by the APOBEC3 (Apolipoprotein B mRNA-Editing Catalytic Polypeptide-like 3 enzymes), which can cause harmful effects on this virus **[(Huang *et al*., 2022) ; (Kumar *et al*., 2022)]**.

Phylogenetically, this Poxvirus was divided into two clades, Congo Basin or Central Africa (CA, Clade I) and West Africa (WA, Clade II) **[(Hraib *et al*., 2022) ; (Gul *et al*., 2022) ; (Xiang & White, 2022)].** A comparative study between the Central African strain (ZAI-96) and three West African strains (SL-V70, COP-58, and WRAIR-61) has revealed a 0.55–0.56% nucleotide difference between the two clades **[(Forni *et al*., 2022) ; (Lum *et al*., 2022) ; (Lansiaux *et al*., 2022) ; (Kumar *et al*., 2022)].** The CA clade is more virulent than the WA clade **[(Bryer *et al*., 2022) ; (Harapan *et al*., 2022) ; (Samaranayake & Anil, 2022)].**

A genomic comparative study between the first WA strain which was isolated in 1971 and another form 2022 MPXV outbreak reported a difference less than 0.06% nucleotide compositions **(Kmiec & Kirchhoff, 2022),** as a result, a novel nomenclature was proposed to classify this virus into three clades, the third one inducing the current outbreak Outside African which has multiples lineages **(Figure 5) (Li *et al*., 2022).**

Another analysis indicated that the Monkeypox virus 2022 outbreak strains contained 46 new consensus mutations, including 24 non synonymous mutations, compared with the

Monkeypox virus-2018 strain, and suggested that the lower mortality and higher transmission of these strains are due to these mutations **(Huang *et al*., 2022).**

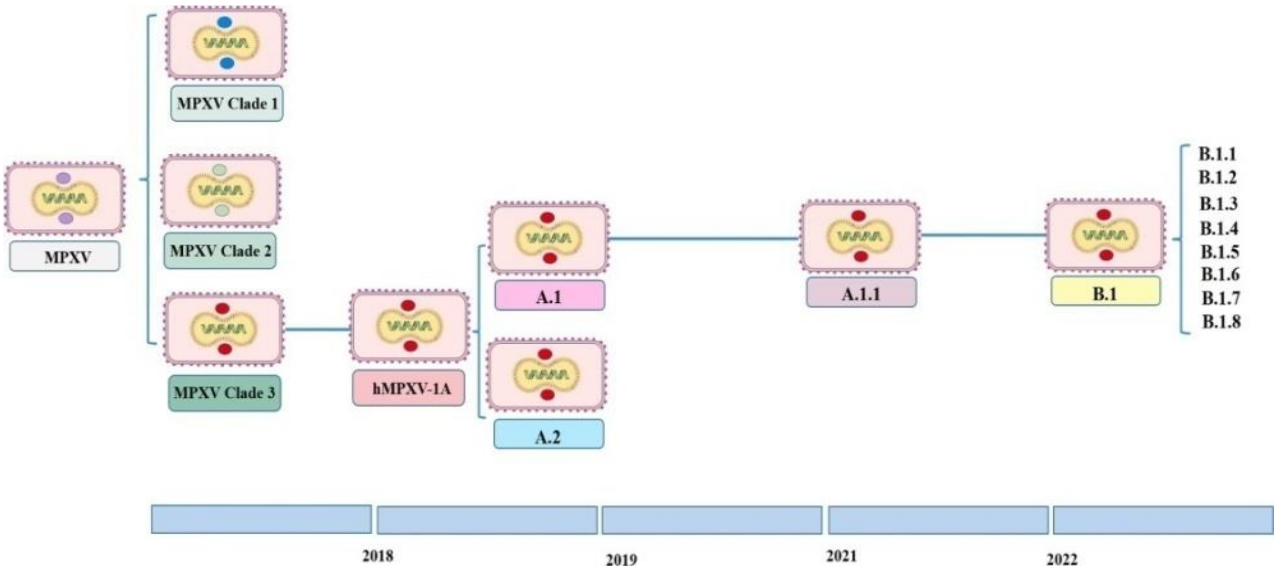


Figure 5: Schematic representations of the major evolutionary events and MPXV variants in sequential order (Li *et al*., 2022).

2.6 Life cycle of the virus

There is no specific tissue tropism of MPXV because it was detected in several tissues **(Alakunle *et al*., 2020).** Initially, it infects lower airway epithelial cells and spreads to lymph nodes, followed by systemic dissemination through Monocytes **(Kmiec & Kirchhoff, 2022).**

Like all Poxviruses, MPXV performs their replication cycle into the cytoplasm of the host cell with the use of a virally encoded RNA polymerase which is uncommon among DNA viruses **[(Huang *et al*., 2022) ; (Kumar *et al*., 2022) ; (Li *et al*., 2022) ; (Titanji *et al*., 2022)].** This viral cycle is carried through multiple steps, including viral particle entry, genomic replication, assembly, and release **(Figure 6) (Li *et al*., 2022).**

2.6.1 Viral entry

Scientists suggest that Monkeypox viral entry is associated with host cell type and viral clade **(Li *et al*., 2022).** To date, the specific receptors of this virus are still unknown **(Li *et al*., 2022)** but several possible glycosaminoglycans cell surface receptors external viral, including Heparin Sulfates and Chondroitin, and Laminin can promote the attachment of this virus on the surface of infected cell **[(Huang *et al*., 2022) ; (Kmiec & Kirchhoff, 2022) ; (Lozano &**

Muller, 2023)]. Next, MPXV enter to the target cell by the use of two different methods, if this particle is found in a neutral medium it will enter by direct fusion, but in low pH, it will use endosomal pathways(macropinocytosis endocytosed) **[(Li *et al*., 2022) ; (Kmiec & Kirchhoff, 2022) ; (Kumar *et al*., 2022)].** Following that, it releases its nucleocapsid (core) into the cytoplasm **(Aljabali *et al*., 2022).**

2.6.2 Replication

In the cytoplasm, this obligate intracellular virus synthesizes early, intermediate, and late viral mRNA through MPXV-encoded multi-subunit DNA-dependent RNA polymerases (RNAPs) and several host transcription factors and proteins **[(Huang *et al*., 2022) ;** (**Li *et al*., 2022) ; (Li *et al*., 2023)].** This stage is followed by the translation of early, intermediate, and late proteins on host ribosome **[(Li *et al*., 2022) ; (Kmiec & Kirchhoff, 2022)].**

2.6.3 Assembly and release

This step consists of assembly and differentiation into Intracellular Mature Virions (IMVs) **(Li *et al*., 2023),** some of them are released externally by cell lysis, and other particles are transported through microtubules toward the endoplasmic reticulum or Golgi to acquire their envelope to be Intracellular Enveloped Viruses (IEVs) which released from this host by exocytosis **[(Li *et al*., 2022) ; (Hatmal *et al*., 2022)].**

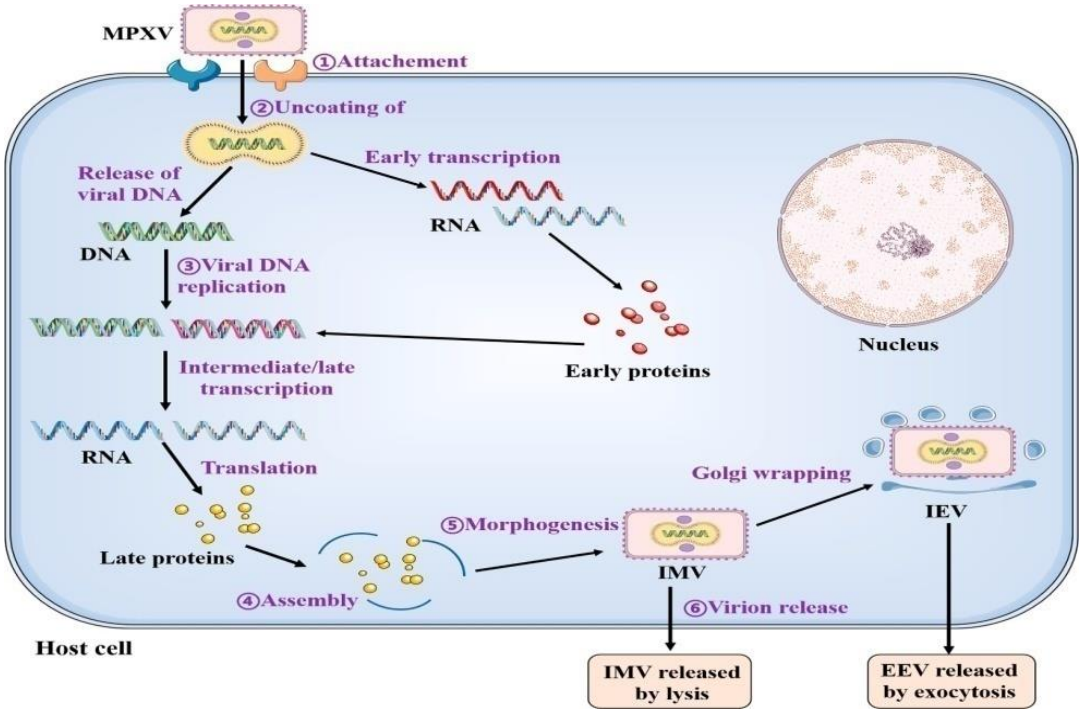


Figure 6 : Replication cycle of the MPXV (Li *et al*., 2022).

2.7 Transmission

Monkeypox virus transmission divides into two modes, animal-to-human, and human-to-human **(Figure 7) [(Luo & Han, 2022) ; (Ranganath *et al*., 2022).** To date, its exact transmission mode is still unknown **(Kaler *et al*., 2022).**

2.7.1 Animal-to-human transmission

In the 1980s in DRC, 72.5% of MKPX-infected cases were the result of this transmission mode **(Ejaz *et al*., 2022).** Persons, who sleep outside or on the ground, reside near a forest, and visit the forest, are the most suspected for this type of transmission **[(Awan *et al*., 2022) ; (Kaler *et al*., 2022) ; (Samaranayake & Anil, 2022)].** They would acquire this zoonotic virus through direct contact with blood or bodily fluids of animals carrying the virus, touching the bidding, and coetaneous or mucosal lesions from bites or scratches of infected animals **[(Alakunle *et al*., 2020) ; (Bryer *et al*., 2022) ; (El Eid *et al*., 2022) ; (Kumar *et al*., 2022) ; (Kaler *et al*., 2022) ; (de la Calle-Prieto *et al*., 2023)].** Moreover, the consumption of raw meat and using infected animal products like bushmeat (wild meat) promote this type of transmission **[(Altindis *et al*., 2022) ; (Gong *et al*., 2022) ; (Titanji *et al*., 2022)].**

2.7.2 Human-to-human transmission

This transmission mode is the causative of the most reported cases in Nigeria outbreaks (between 2017 and 2018) **(Ejaz *et al*., 2022).** Monkeypox virus can transmit between humans through direct contact, muco-cutaneous lesions, body fluids, and sustained respiratory droplets exposure within six feet for three hours or more **[(Hraib *et al*., 2022) ; (Johri *et al*., 2022) ; (Kumar *et al*., 2022) ; (Kaler *et al*., 2022) ; (Ranganath *et al*., 2022)].** Additionally, Physical contact with contaminated objects or surfaces, eating or drinking from the same dishes of an infected individual plays decisive role in Monkeypox spread **[(Altindis *et al*., 2022) ; (El Eid *et al*., 2022) ; (Kaler *et al*., 2022) ; (Tiwari *et al*., 2023)].**

This Poxvirus has proven its high ability to transmit through sexual relations, especially homosexuals, where the WHO has reported that between 55561 confirmed cases, 89% of them acquired this virus from unsafe sexual activities with men **[(Ejaz *et al*., 2022) ; (Gong *et al*., 2022) ; (Lu *et al*., 2022) ; (Tiwari *et al*., 2023)].**

Otherwise, parents that are infected by MPXV can transmit it to their baby through two ways, vertical transmission during pregnancy, and close skin contact **[(Altindis *et al*., 2022) ; (El Eid *et al*., 2022) ; (Kumar *et al*., 2022) ; (Li *et al*., 2022) ; (Zhu *et al*., 2022)].**

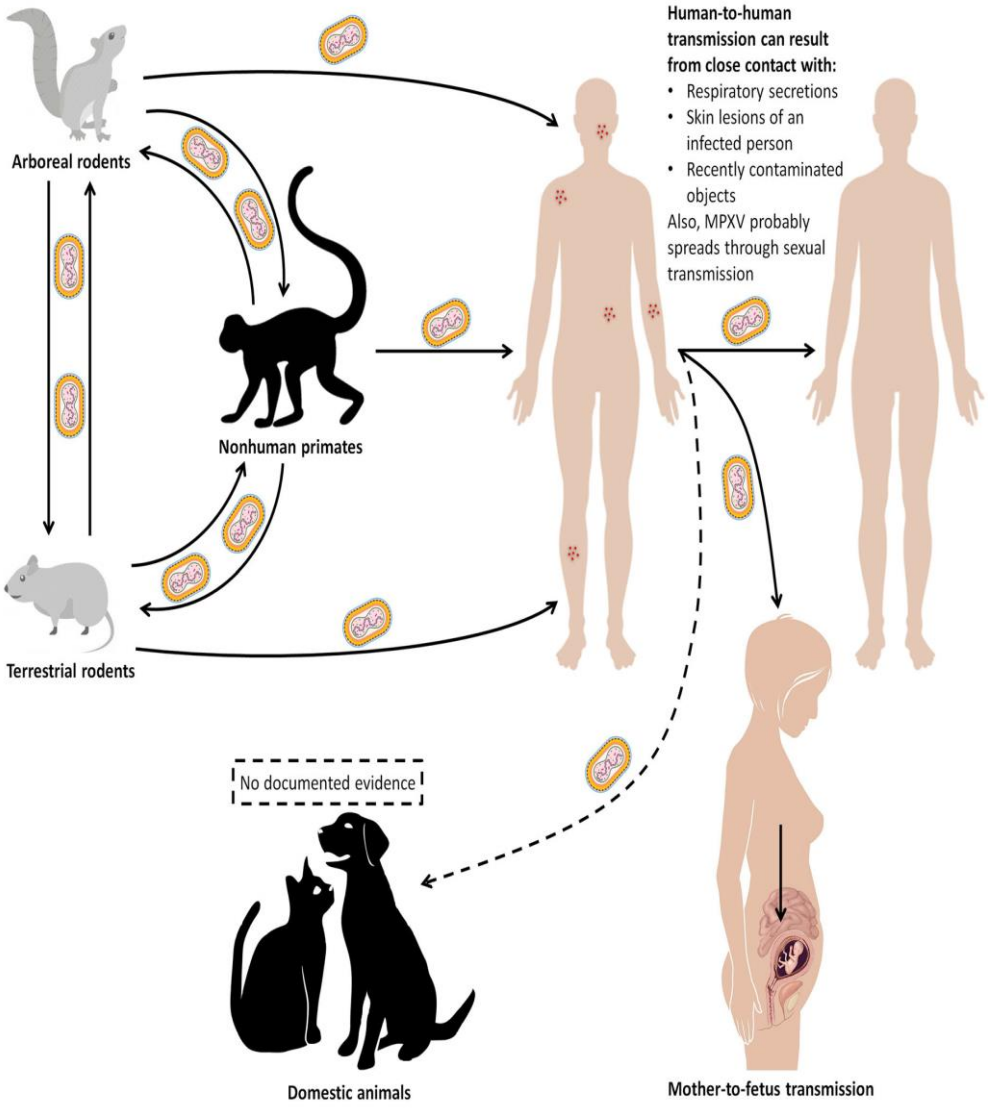


Figure 7: Modes of Monkeypox transmission (Hatmal *et al*., 2022).

Chapter Three: Monkeypox Disease

Monkeypox (MPX) is a highly contagious infectious disease **(Samaranayake & Anil, 2022)** which appears on the WHO list of infectious diseases caused by viruses that have the potential to be endemic or pandemic **(Shafaati & Zandi, 2022).**

1. Incubation

In virology, the incubation period was defined as the non-contagious period between the viral entry into the body and the appearance of the first symptoms **[(Sims & Epp, 2021) ; (Johri *et al*., 2022) ; (Kaler *et al*., 2022) ; (Luo & Han, 2022)].** For Monkeypox disease, this asymptomatic period was estimated to be 7.4 days (ranging from five days to three weeks); (most likely 7 to 14 days) **[(Ajmera *et al*., 2022) ; (del Rio & Malani, 2022) ; (El Eid *et al*., 2022) ; (Hraib *et al*., 2022) ; (Kumar *et al*., 2022) ; (Onchonga, 2022) ; (de la Calle-Prieto *et al*., 2023)].**

2. Symptoms

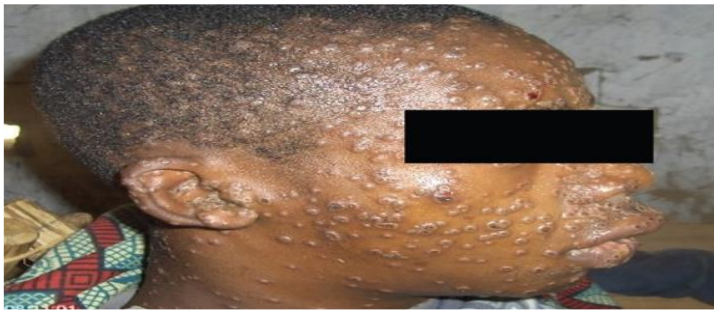
This dangerous infection can be divided into two periods, the invasion period (prodromal) and the skin eruption period (rash phase) **(Luo & Han, 2022).**

The prodromal phase which is estimated from 1 to 5 days **[(Ejaz *et al*., 2022) ; (Luo & Han, 2022) ; (Ranganath *et al*., 2022)]** is characterized by the onset of fever, restlessness, and unilateral or bilateral lymphadenopathy which defined as enlargement of lymph nodes beyond its normal stat in submandibular, cervical, postauricular, axillary, and inguinal places, which grows from 1 cm to 4 cm **[(Hanif *et al*., 2009) ; (Damon, 2011) ; (Bertholom, 2022) ; (Hraib *et al*., 2022) ; (Lam *et al*., 2022) ; (Lu *et al*., 2022) ; (Ranganath *et al*., 2022)].** Moreover, this invasion period can also be associated with other general signs like severe headaches, muscle and back aches, chills, exhaustion, asthenia, and vomiting **[(Ahmed *et al*., 2022) ; (Billioux *et al*., 2022) ; (Ejaz *et al*., 2022) ; (Luo & Han, 2022) ; (Ranganath *et al*., 2022)].** Therefore, There is a high similarity between the symptoms of Monkeypox, smallpox, measles, and chickenpox, and lymphadenopathy is the only symptom that distinguishes MPX from the others **[(Altindis *et al*., 2022) ; (Harapan *et al*., 2022) ; (Hraib *et al*., 2022) ; (Titanji *et al*., 2022)].**

After the first period, the Monkeypox infection enters the rash phase, which progresses from 2 to 4 weeks **[(Huang *et al*., 2022) ; (Gong *et al*., 2022)].** This phase is characterized by the onset of pleomorphic rash **(Figure 8),** which generally starts in the face and then spreads quickly to the whole body, including palms and soles of the feet, oral mucosa, genitals, and conjunctiva **[(Ejaz *et al*., 2022) ; (Gong *et al*., 2022) ; (Lu *et al*., 2022) ; (Ranganath *et al*.,**

2022)]. Usually, the number of these lesions is between 1 and 100 while its diameter range is 0.5cm but sometimes can get up to 1cm **[(Hraib *et al*., 2022) ; (Singhal *et al*., 2022)].**

Figure 8: Patient with Smallpox showing characteristic lesions (McCollum & Damon, 2014).



According to the results of some studies, scientists suggest that infected persons can suffer from the rash before other symptoms or can only experience a rash **[(Altindis *et al*., 2022) ; (Khudhair, 2022) ; (Sah *et al*., 2022)].** Also, they suggest that this infection might be asymptomatic in some populations according to a serological study during the Cameron MPX outbreak where they find many individuals who did not show any symptoms had a high titer of Orthopoxvirus Immunoglobulin G (IgG) and Immunoglobulin M (IgM) antibodies **(Harapan *et al*., 2022).**

3. Complications

Monkeypox infection can be accompanied by a range of complications such as bronchopneumonia, cardiovascular involvement, extra-cutaneous manifestations like secondary skin soft tissue infection, bacterial superinfections and gastrointestinal involvement as vomiting, diarrhea with dehydration **[(Hraib *et al*., 2022) ; (Gong *et al*., 2022) ; (Johri *et al*., 2022) ; (Kaler *et al*., 2022) ; (Luo & Han, 2022) ; (Pastula & Tyler, 2022) ; (Li *et al*., 2022)].**

Additionally, ophthalmic manifestations like conjunctivitis, blepharitis, keratitis, or corneal lesions represent rare serious long MPX complications that can cause loss of vision **[(Huang *et al*., 2022) ; (Kmiec & Kirchhoff, 2022) ; (Abdelaal *et al*., 2023)].** Often, severe neurological complications such as encephalitis, seizures, cranial nerve palsy, Guillain-Barre syndrome, hemiplegia, and coma can be observed in some Monkeypox-infected cases **[(Billioux *et al*., 2022) ; (Shafaati & Zandi, 2022) ; (Tiecco *et al*., 2022)].** Moreover, Patients can also suffer from significant psychological distress, and recently, the WHO called for greater attention to mental health problems and suicide prevention during epidemics **[(Huang *et al*., 2022) ; (Tiecco *et al*., 2022)].**

Therefore, This complications are more common in younger children (more than eight years) and adolescents, pregnant women, homosexual and bisexual males, and patients with immunocompromising, particularity those with AIDS **[(Sims & Epp, 2021) ; (Ajmera *et al*., 2022) ; (Ejaz *et al*., 2022) ; (Hatmal *et al*., 2022) ; (Luo & Han, 2022) ; (Mohapatra *et al*., 2022) ; (Nuzzo *et al*., 2022) ; (Ranganath *et al*., 2022) ; (Mills *et al*., 2023)].**

4. The immune system response to Monkeypox

Monkeypox virus entry into the target cells triggers a classical immune response against it by the use of both arms of the immune system, innate and adaptative immune **(Ejaz *et al*., 2022).**

4.1 Innate Immunity

To date, the effective roles of innate immune cells like monocytes, macrophages and innate lymphoid cells are still unknown **(Lozano & Muller, 2023).**

The feature of innate immunity lies in the presence of Pattern Recognition Receptors (PRRs) which are used to initiate an immune response cascade **[(Hakim & Widyaningsih, 2023) ; (Ophinni *et al*., 2022)],** and it represents the first line of defense following active viral infection **(Lum *et al*., 2022).**

Many cells play key roles in this immune response such as Natural killer cells which modulate the functions of other immunity cells like T cells through cytokines secretions **[(Alakunle *et al*., 2020) ; (Ejaz *et al*., 2022) ; (Lum *et al*., 2022)],** and Dendritic cells (antigen-presenting cells) which migrate to viral replications sites to activate other immune cells **(Saghazadeh & Rezaei, 2022).** Moreover, this Complex System perform a variety of functions, including the removal of cellular debris, the initiation of an inflammatory response, the activation of adaptive immunity, and the recognition of virus-infected cells **(Li *et al*., 2023).**

4.2 Adaptive immunity

After the innate immunity, the virus leads to activate adaptative immunity which occurs proximally between 7 to 14 weeks and 1 year after exposure, initially cellular then humoral **[(Bohelay & Duong, 2019) ; (Lozano & Muller, 2023)].**

At the start of the MPX infection, two types of T-cells are involved, Lymphocytes T auxiliary CD4+(LT4) which recruits Lympogocytes T auxiliary CD8+ (LT8) to the sites of viral replication and favorite its differentiation into effectors and memory T cells, and this

LT8 kills the infected cells through indirect induction of killing cytokines, like Interferon-gamma (IFN-γ) and Tumor Necrosis Factor α (TNF-α), or directly through cell-to-cell contact **(Saghazadeh & Rezaei, 2022).**

Subsequently, the second stage of immune defense takes place under the surveillance of B cells which differentiate into plasma cells that in turn, migrate to immune organs like the lymph nodes, mucus membranes, and bone marrow to produce specific antibodies against MPXV and facilitate their entry to the bloodstream to control the viral spread **[(DeFranco *et al*., 2009) ; (Saghazadeh & Rezaei, 2022)].**

4.3 Immune evasion

Like other *Orthopoxviruses*, the Monkeypox virus develops many different mechanisms to evade or worsen host immune responses **(Figure 9) [(Alakunle *et al*., 2020) ; (Harapan e*t al*., 2022)].** This emerging virus improves its ability to prevent apoptosis in infected cells by expressing specific proteins which that target the apoptotic pathways **(Lum*et al*., 2022).**

Moreover, the MPXV genome encodes multiples proteins that promote its immune evasion like B16 which inhibits antiviral type I interferon-induced signaling **(Kmiec & Kirchhoff, 2022),** and A47R which interacts with specific adaptor proteins to inhibit the transcription factors associated with inflammation like the Nuclear factor-κB (NF-κB) **(Harapan *et al*., 2022).**

In addition, this pathogen can inhibit the Natural killer cells activities by interfering with their activation processes **(Lum *et al*., 2022).** As well, The Central African MPXV Zaire strain can expresses the Monkeypox Inhibitor of Complement Enzymes (MOPICE) coded by the D14 gene which blocks the activation of the complement cascade **[(Lum*et al*., 2022) ; (Li *et al*., 2023)].**

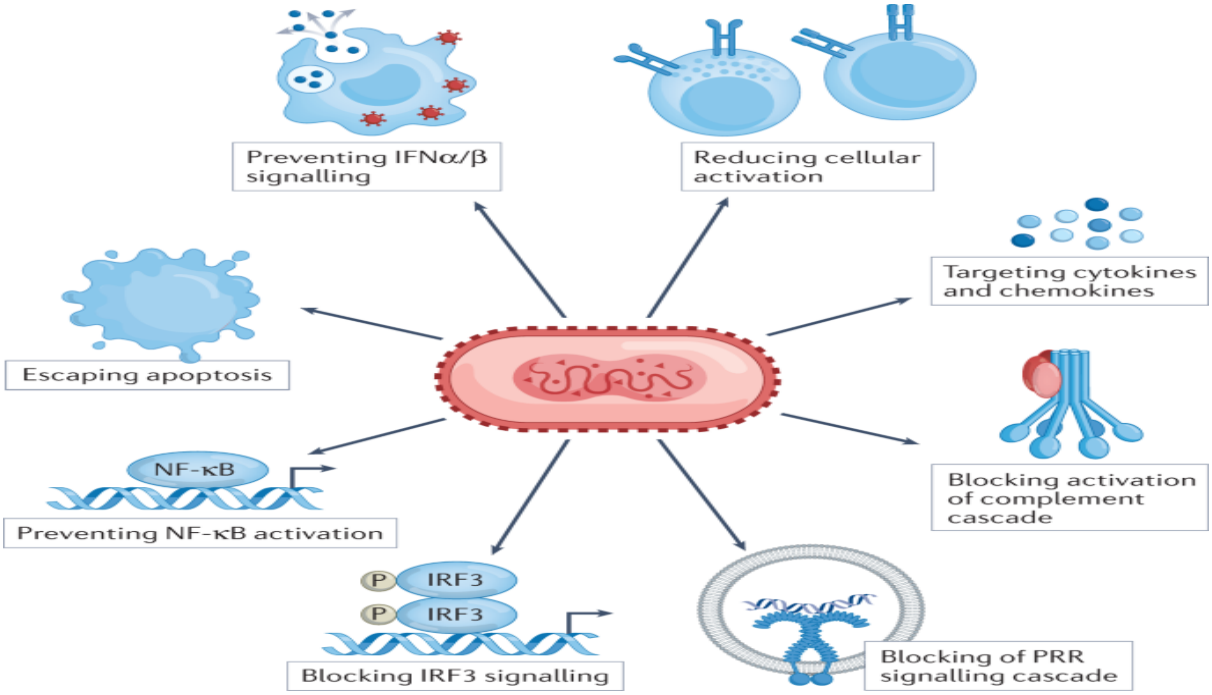


Figure 9: Immune evasion by MPXV (Lum *et al*., 2022).

5. Tests and diagnostic

Diagnostic testing, which is currently performed at the Centers for Disease Control and Prevention (CDC) or State Health Departments (SHD) **(Ranganath *et al*., 2022)** is very important to detect the early stage of infection and to control actual outbreaks **[(Jiang *et al*., 2022) ; (Tiecco *et al*., 2022)].** Usually, the diagnostic efficiency depends on the specimens that should be taken from skin exudates, vesicular lesions, or crusts and kept cold in a sterile and dry tube, and the type of laboratory test **[(Hatmal *et al*., 2022) ; (Luo & Han, 2022)].** Virological diagnosis and detection has many approaches **(Weinstein *et al*., 2005)**

5.1 Serology

The specific IgM and IgG antibodies in the serum of MPX patients after five and eight days of infection can be detected by the use of ELISA technique (Enzyme-linked ImmunoSorbent Assay) **[(Alakunle *et al*., 2020) ; (Singhal *et al*., 2022) ; (Tiecco *et al*., 2022)].** Scientifically, a positive IgM indicates a recent exposure to *Orthopoxvirus* in both vaccinated and unvaccinated people, while a positive IgG indicates a previous exposure to *Orthopoxvirus* from either immunization or infection **(Ejaz *et al*., 2022).**

This serological technique should not be used alone for diagnosis **(Luo & Han, 2022)** because of cross-reactivity between *Orthopoxviruses* and the possibility for false-positive results in those with prior smallpox vaccination **[(El Eid *et al*., 2022) ; (Ranganath *et al*.,**

2022)], but it is very useful for the epidemiological purpose, especially for monitoring Monkeypox epidemics in non-endemic areas **(Forni *et al*., 2022)** due to its rapid detection, simple operation, lack of the need for special equipment, and low cost **(Wang e*t al*., 2020).**

5.2 Electron microscopy observation

Electron microscopy can be used to visualize potential Poxvirus in a sample **(Luo & Han, 2022).** Unfortunately, this method is limited because it is expensive, the operation is extremely complex and takes time **(Gong *et al*., 2022),** and it cannot differentiate MPXV from other Poxvirus due to the great morphological similarity between themes **(Alakunle *et al*., 2020).**

5.3 Nucleic acid detection technology

Real-Time Reverse-Transcription Polymerase Chain Reaction (RT-PCR) principle is based on the detection of specific components of the MPXV genome like conserved regions of extracellular envelope protein gene (B6R), DNA polymerase-gene E9L, DNA-dependent RNA polymerase subunit 18 (RPO18) genes, and complement binding protein C3L, F3L, and N3R **[(Gong *et al*., 2022) ; (Tiecco *et al*., 2022)].**

According to the WHO,RT-PCR is the preferred method for this emerging virus detection **(Kumar *et al*., 2022)** due to its efficiency, sensitivity, and shows positivity from 2 days to 20 days (median 5 days) after the onset of clinical symptoms **[(Ejaz *et al*., 2022) ; (Harapan *et al*., 2022)].** But, the difficulties of RT-PCR lie in the need for high-quality labs which are hard to be found in low resources countries **(Hraib *et al*., 2022).**

Moreover, some Real Time PCR can discriminate between the two MPXV clades **(Tiecco *et al*., 2022),** and it can be used in combination with others technique as Recombinase Polymerase Amplification (RPA), Loop-Mediated Isothermal Amplification (LAMP) technology, and Restriction-Fragment-Length Polymorphism (RFLP)**[(Li *et al*., 2022) ; (Lansiaux *et al*., 2022) ; (Singhal *et al*., 2022)].**

6. Preventive and therapeutic approaches

To fight the Monkeypox infection, it is necessary to find supportive care and symptomatic treatments **(Ejaz *et al*., 2022).** To date, there are no specifically approved treatments by the US Food and Drug Administration (US-FDA) for this contagious infection **(Titanji *et al*., 2022).**

6.1 Drugs

Due to the genetic and antigenic similarity between *Orthopoxviruses* **(Letafati & Sakhavarz, 2023),** Smallpox antiviral drugs like Tecovirimat, Brincidofovir, and Vaccinia Immune Globulin Intravenous (VIGIV) might be beneficial for treating Monkeypox **(Hakim & Widyaningsih, 2023),** although it causes undesirable side effects which are mentioned in **(table 2).**

6.1.1 Tecovirimat (ST-246, TPOXX)

Tecovirimat is an oral intracellular inhibitor drug **[(Gong *et al*., 2022) ; (Kaler *et al*., 2022)]** which was approved by the US-FDA for the treatment of Smallpox in adults and children **[(Luo & Han, 2022) ; (Ranganath *et al*., 2022)].** Therefore, it was licensed in 2022, by the European Medicines Agency (EMA) to treat MPX infection. the drug blocks the final step of virus maturation by targeting the Vp37 viral protein which is responsible for the virulence through the formation of the viral envelope and the release of this mature virus into the outer environment **[(Aljabali *et al*., 2022) ; (de la Calle-Prieto *et al*., 2023)].**

6.1.2 Cidofovir (Vistide)

Cidofovir is an acyclic nucleoside monophosphate (cytosine analogue) **(Huang *et al*., 2022).** It was approved by the FDA in 1996, to treat Cytomegalovirus (CMV) retinitis in people with AIDS **[(Johri *et al*., 2022) ; (Titanji *et al*., 2022)].** Thus, The US-CDC allowed this drug to treat *Orthopoxviruses* during the outbreak **[(Bryer *et al*., 2022) ; (Luo & Han, 2022)],** it gave positive results when scientists tested its ability to treat this virus in an animal model **(Ranganath *et al*., 2022).** Hence, at the cellular level, this medicament was transformed into Cidofovir-diphosphate (CDV-PP) which inhibits the synthesis of viral DNA polymerase in the form of a substitute matrix and eventually blocks viral DNA synthesis at the DNA polymerase level **(Gong *et al*., 2022).**

6.1.3 Brincidofovir (CMX001, Tembexa)

CMX001 is a lipid conjugate of Cidofovir **(Li *et al*., 2023)** which is characterized by a very long half-life and greater selective index (SI)* which was at least 25-fold higher than Cidofovir **[(Oliveira *et al*., 2018) ; (Alakunle *et al*., 2020) ; (de la Calle-Prieto *et al*., 2023)].** It was approved by the EMA and the US FDA to treat Smallpox in adults and children, including newborns **[(Luo & Han, 2022) ; (Titanji *et al*., 2022)].** In addition, it acts by inhibiting DNA polymerase after incorporation into viral DNA **(de la Calle-Prieto *et al*., 2023).**

*****SI: the relationship between the antiviral dose necessary to reduce in 50% the virus replication (EC50) and cytotoxic dose (CC50), the value obtained in SI allow estimating drug safety level for use in animals

6.1.4 Vaccinia Immune Globulin Intravenous (VIGIV)

VIGIV is licensed by the FDA for the treatment of complications due to vaccinia vaccination, including eczema vaccinatum, progressive vaccinia, and severe generalized vaccinia **[(Tiecco *et al.*, 2022) ; (Titanji *et al.*, 2022)].** This drug contains the pooled polyclonal immunoglobulin's that have been purified from the plasma of thousands of healthy donors **(Li *et al.*, 2023).** Immunologically, it improves the immune response by decreasing macrophage activity, reducing endogenous antibody production, inhibiting auto-reactive T cells, and a balanced cytokine profile **(Li *et al.*, 2023).** The CDC has an expanded access protocol that authorizes the use of VIGIV to treat Orthopoxviruses during an outbreak, but to date, there is no evidence that VIG is effective against Monkeypox **(Johri *et al.*, 2022).**

Table 2: Side effects of potential drugs for Monkeypox Infection (Titanji *et al.*, 2022).

Drug	Side effects and Adverse Events
Tecovirimat	Intravenous use: pain and swelling at infusion site, extravasations at infusion site, headache. Oral use: headache, abdominal pain, nausea, vomiting.
Cidofovir	Nephrotoxicity, neutropenia, decreased intraocular pressure, nausea, vomiting
Brincidofovir	Abdominal pain, nausea, vomiting, diarrhea, elevated liver transaminases and bilirubin
VIGIV	Infusion reaction; local injection-site reaction (contraindicated in persons with IgA deficiency and possible IgA hypersensitivity)

6.2 Vaccines

Monkeypox vaccines represent the second and the third generation of the smallpox vaccines, which has gone by the use of medical technology (**Mitjà *et al.*, 2023).**

The US and the UK were the first countries to pursue vaccination to close contacts of MPX cases in the 2003, 2018 and 2019 outbreak. Afterwards, more and more countries like Canada decided to offer vaccination to people exposed to MPXV or at risk of acquiring it **[(Kupferschmidt, 2022) ; (Kmiec & Kirchhoff, 2022)].**

6.2.1 Second-generation vaccine (ACAM 2000)

ACAM 2000 is a live vaccinia virus preparation **(Lu *et al*., 2022)** that was demonstrated in the US, in 2003, to reduce MPXV symptoms during the outbreak (**Gong *et al*., 2022).** Subsequently, its use was licensed by the FDA in August 2007, **(Rizk *et al*., 2022).** So, the Strategic National Stockpile (SNS) has over 100 million doses of ACAM2000 that are immediately available in its inventory **(Aljabali *et al*., 2022).**

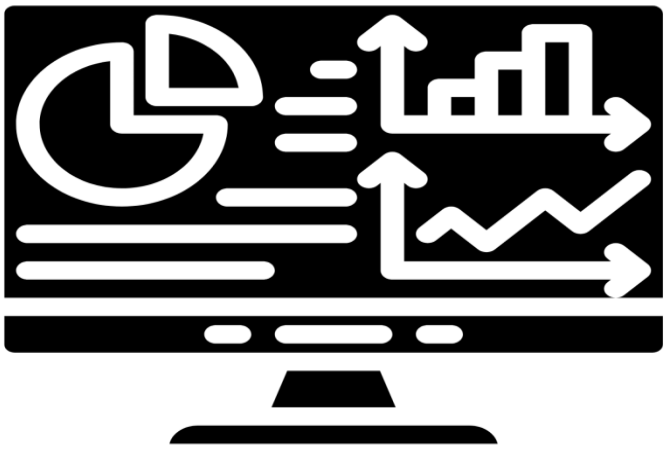
This vaccine involves one dose and peak vaccine protection is conferred within 28 days **(Tiecco *et al*., 2022).** It can cause lesions in injection sites which can spread to other sites or peoples, while also carrying the potential for adverse outcomes like progressive vaccinia, eczema vaccinatum, and myopericarditis **(Johri *et al*., 2022),** as a result, it is not available to the public, especially for individuals with immunodeficiency such as atopic dermatitis and AIDS, and in MPXV endemic areas **[(Li *et al*., 2023) ; (Gong *et al*., 2022)].**

6.2.2 Third generation vaccine (JYNNEOS and IMVAMUNE)

JYNNEOS is a live viral vaccine produced from the modified vaccinia Ankara-Bavarian Nordic (MVA-BN strain) **(Rizk *et al*., 2022).** It can cross-react and generates immune protection against MPXV **(Aljabali *et al*., 2022),** and in 2019, the US FDA approved the use of this vaccine against emerging diseases **(Lai *et al*., 2022).** As a result , The U.S. recently distributed 1200 doses of the JYNNEOS vaccine from its national stockpile across the U.S. for people who have had high-risk exposures to Monkeypox **(Aljabali *et al*., 2022).**

This vaccine involves two vaccine doses 28 days apart, and vaccine protection is not conferred until two weeks after receipt of the second dose **(Tiecco *et al*., 2022),** and it can be used in patients with atopic dermatitis and immunodeficiency persons **(Gong *et al*., 2022).** Finally, in June 2022, over 300,000 doses have been distributed mainly, among males aged 25-39 years **(Ophinni *et al*., 2022).**

Experimental Part



1. Methodology

The emergence and the growing number of Monkeypox virus cases worldwide pose a serious threat to human life, especially in non-endemic countries like Algeria. Additionally, the general poor public understanding of Monkeypox, which makes it a prerequisite for controlling and preventing this zoonotic virus and its disease **(Dong *et al*., 2023).**

1.1 Objective

The purpose of our study is to evaluate knowledge of teachers, administrative workers and students of the Faculty of Natural and Life Sciences and Earth and Universe Sciences of University of Tlemcen (NLS/EUS: SNV/STU) about this contagious virus in order to promote awareness about the disease and its transmission for anticipating any outbreak in Algeria.

1.2 Type of the study

This study was designed as a cross-sectional web-based survey that took place in the Faculty of SNV /STU at the University of Tlemcen **(Appendice 1)**. Launched for a 20 days period, while having 125 voluntary participants from five different departments of our faculty including Biology, Ecology and Environment, Earth Sciences and Universe, Agronomy, and Forest Resources.

Our survey was created on Google Forms platform in the French language to make it more understandable for the participants of our faculty. It was divided into two different sections, sociodemographic characteristics section and MPXV and disease knowledge's section, respectively with 25 interrogations, where it was shared through mail and social media platforms such as Facebook.

1.3 Data analysis

The statistical analysis was performed using the statistical software SPSS (Statistical Package for Social Sciences) version 25 and Microsoft Office Excel 2007, as well as the creation of tables and graphs.

2. Results and Interpretation

In this section, results obtained from the survey were interpreted according to the following criteria.

2.1 Socio-demographic criteria

2.1.1 Distribution by age and Gender

The results indicate that the majority of respondents were women and belonged the 21-40 years' age group (46.4%) **(Table 3).** These results may be explained by the fact that younger generations use more of social media than others, and more specifically, females that are interested in learning about the latest developments in the field of health.

Table 3: Distribution by age and Gender.

Age	Gender		Total
	Males	Females	
≥20	1.6%	14.4%	16%
21 – 40	5.6%	46.4%	52%
41 – 60	12.8%	18.4%	31.2%
61– 80	0.8%	00%	0.8%
Total	20.8%	79.2%	100%

2.1.2 Distribution by status and departments

The table below **(Table 4)** shows that biology students were the most interactive with this study, as they marked the highest participation rate estimated at 45.6%. This can be explained by the fact that students, more especially biologists that were considered the most active in our study pass more time on social networking websites than others.

Table 4: Distribution by Status and Faculty departments.

Status	Departments					Total
	Biology	Agronomy	Ecology and Environment	Forest Resources	Earth and Universe Science	
Teacher	27.2%	1.6%	8%	1.6%	5.6%	44%
Student	45.6%	1.6%	0.8%	00%	6.4%	54.4%
Administrative-worker	1.6%	00%	00%	00%	00%	1.6%
Total	74.4%	3.2%	8.8%	1.6%	12%	100%

2.2 Criteria on knowledge of Monkeypox virus and its disease

2.2.1 Distribution according to the knowledge that the causative agent of this disease is a virus

Figure below **(Figure 10)** shows that most of the participants (90%) previously knew that this disease is related to a virus. These results are consistent with precedents studies carried out in Indonesia **(Harapan *et al*., 2020),** Nigeria **(Ugwu *et al*., 2022),** China **(Ren *et al*., 2023),** and Jordan **(Al Mse`adeen *et al*., 2023).**

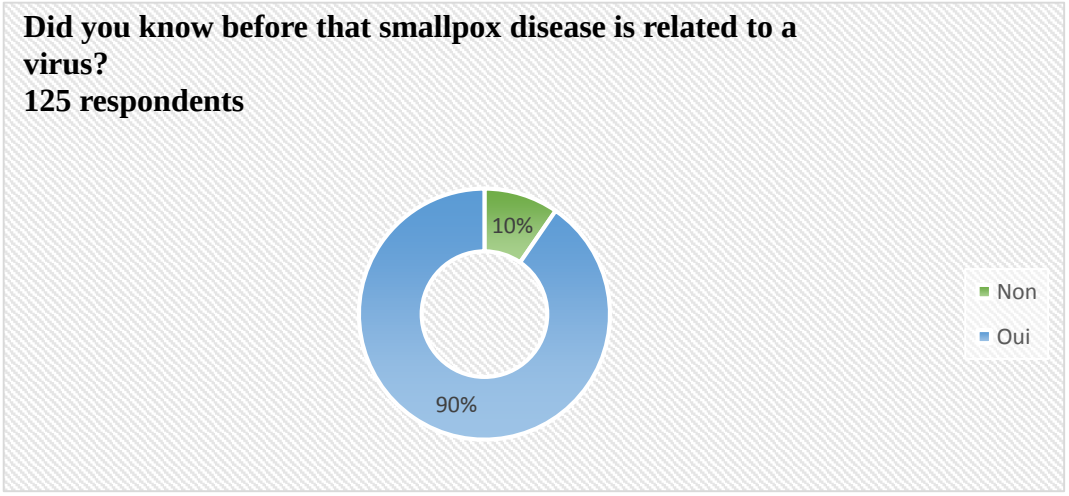


Figure 10: Distribution according to the knowledge that the causative agent of this disease is a virus.

2.2.2 Distribution according to the knowledge of the emergence of the new Monkeypox virus

Among the 125 participants, more than two-thirds (61%) have heard about the emergence of the new Monkeypox virus before completing this questionnaire **(Figure 11), Youssef *et al*. (2023),** also found the same result in their study from Lebanon **(Lin *et al*., 2022).** It could be explained by the fact that this virus caused several outbreaks in African and non-African countries so it becomes a topic of news in social media.

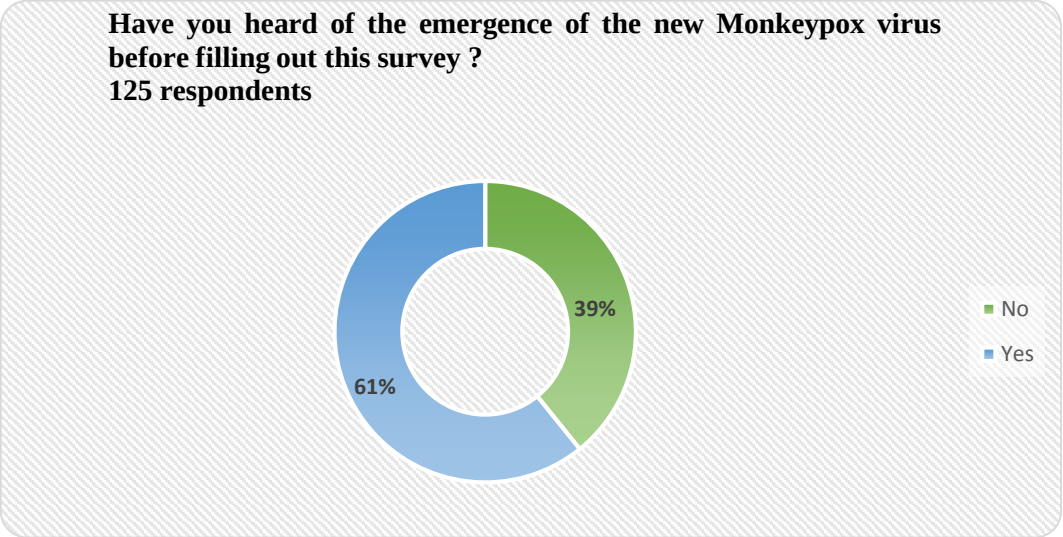


Figure 11: Distribution according to the knowledge of the emergence of the new Monkeypox virus.

Our data suggests that among the 76 participants who have heard about the emergence of this virus, more than half of theme (59.1%) received their information from social media **(Figure 12).** These results are consistent with three previous studies which were carried out in different countries, Indonesia **(Harapan *et al*., 2020),** Saudi-Arabia **(Alshahrani *et al*., 2022)** and Iraq **(Ahmed *et al*., 2023).** Remarkably, this result is considered as the biggest evidence of the importance of social networking sites and their great role in spreading awareness and the latest scientific developments.

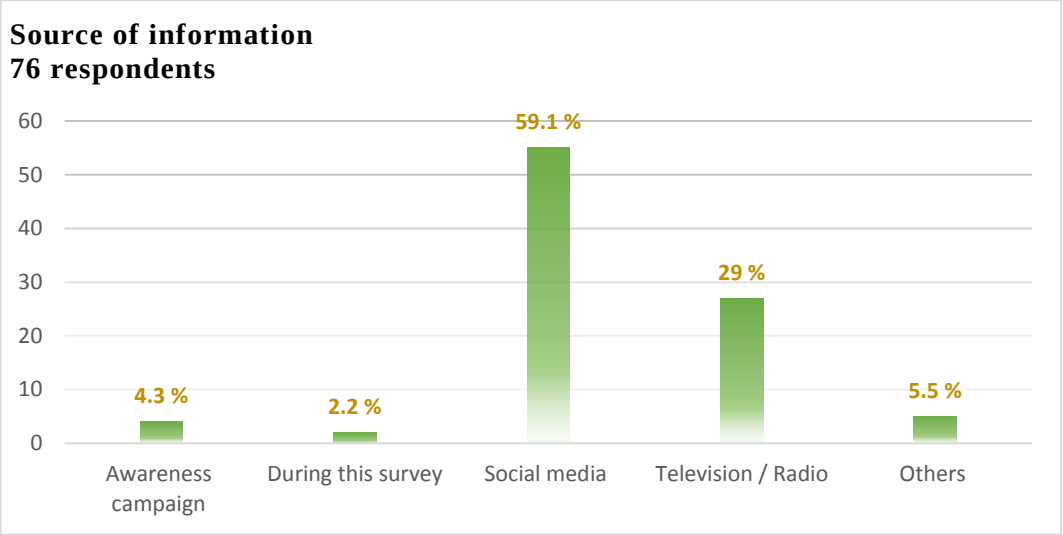


Figure 12: Distribution by source of information.

2.2.3 Distribution according to the belief of the existence of this virus

Our results found that 86 respondents (69%) believe in the existence of this virus **(Figure 13).** The result is also in line with a previous study done at a Malaysian dental school**(Lin *et al.*, 2022).** This might show that the emergence of SARS-CoV-2 and its drastic consequences brought more widespread attention and belief to other emerging viruses and diseases.

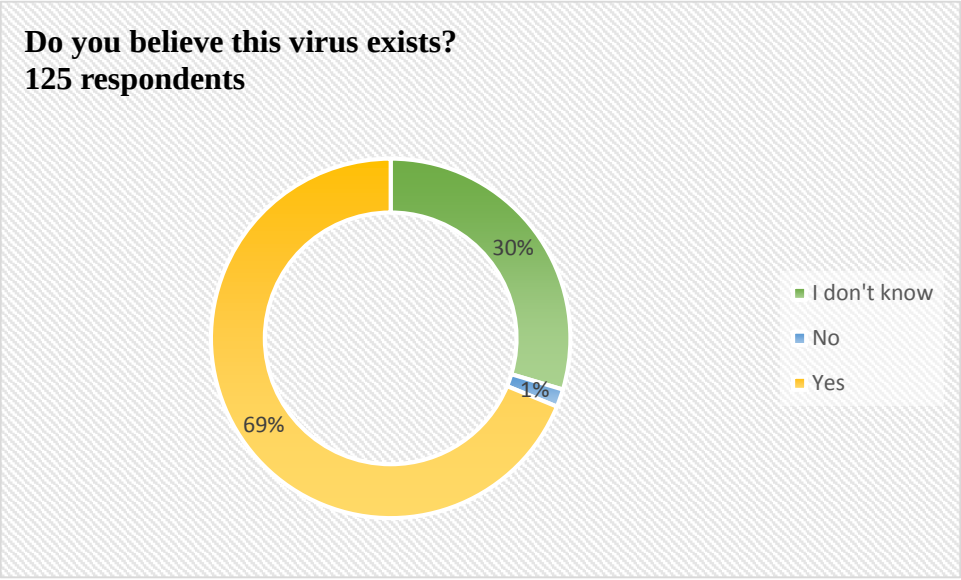


Figure 13: Distribution according to the belief of the existence of this virus.

2.2.4 Distribution according to virus origin

Only 15% of our respondents agreed that this virus is not natural, contrary to 34% of them who think the opposite **(Figure 14).** According to literature, there are several studies

which prove that Monkeypox virus is a close relative of Variola virus (> 90% genome homology) and that its origin is a wild animal **[(Quiner *et al.*, 2017) ; (Kaler *et al.*, 2022) ; (Mileto *et al.*, 2022)].**

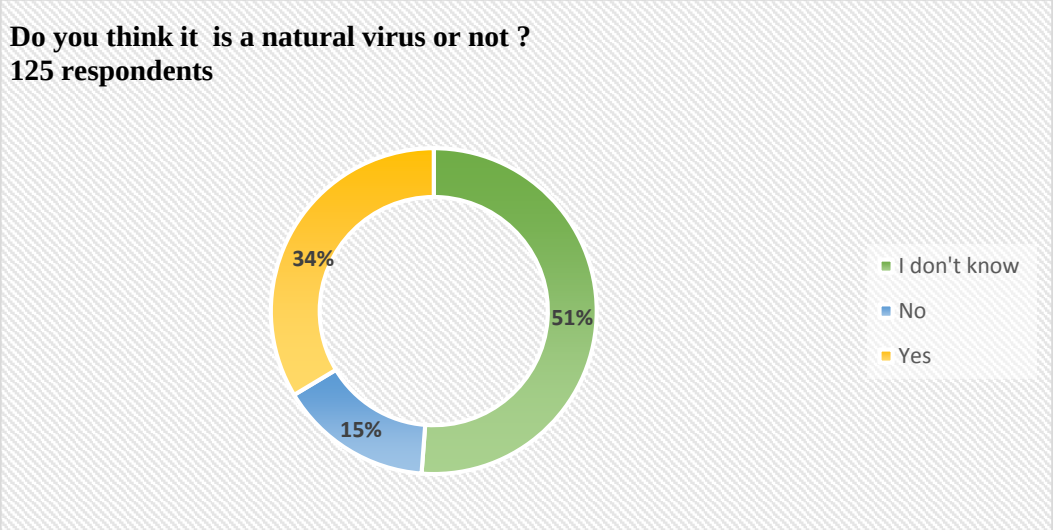


Figure 14: Distribution according to virus origin (Natural or not).

2.2.5 Distribution according to the knowledge of its main sources of transmission

The answers of the respondents about the modes of the Monkeypox virus transmission show that just 47% of acknowledge knowing them **(Figure 15).** This relatively limited information can be explained by the fact that Algeria has not yet been exposed to an epidemic of this virus.

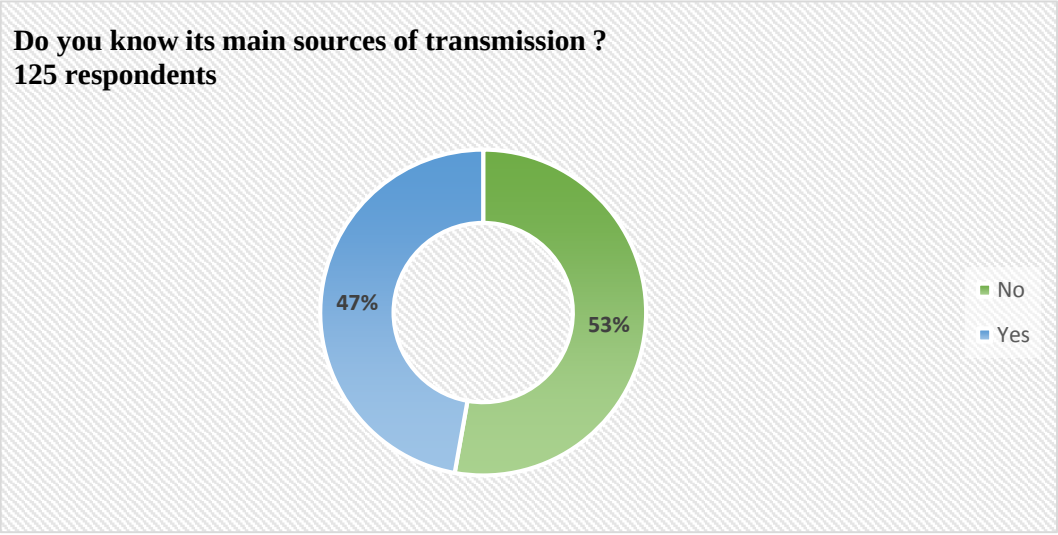


Figure 15: Distribution according to the knowledge of its main sources of transmission.

This zoonotic virus can transmit through many routes **(Kaler *et al.*, 2022).** As a result, all of these transmission routes may be present in combination, for that it is difficult to distinguish between them in any given individual exposure or outbreak scenario **(Kwok *et al.*, 2022).** In our study we found that among the 66 respondents who declared knowing the sources of transmission of the virus, the majority strongly agreed that Monkeypox could be transmitted through contact with an infected animal or person (31.1%, 30%, respectively) **(Figure 16).**

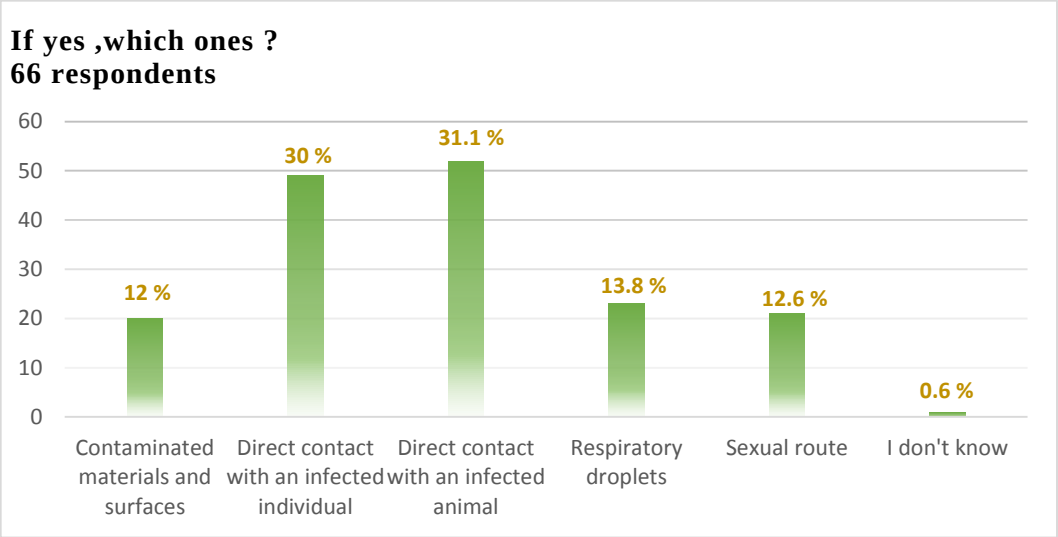


Figure 16: Distribution according to main sources of transmission.

2.2.6 Distribution according to knowledge about the rapid transmission of this virus from a person to another

Through the Figure below **(Figure 17)** almost half of participants (43%) did not know if MPXV does spread easily between people or not, and only 39% of them were aware that this virus does spread easily between people, which is in agreement with a previous study conducted in Saudi-Arabia in 2022, where only 41.9% of the participants unanimously agreed on the ease of its transmission between people**(Alshahrani *et al.*, 2022).** Historically, the virus did not spread efficiently between humans, requiring direct contact with infected body fluids or fomites (bed sheets) or sustained respiratory droplet exposure within 6 meters for 3 hours or more **(Ranganath *et al.*, 2022),** but recently this emerging virus has proven its great ability to spread among people, and the biggest evidence was in May 2022 where more than over 17,300 confirmed and suspected cases were identified**,** and over 40.000 infected people in 87 countries that were not MPXV endemic **[(Gomez-Garberi *et al.*, 2022) ; (Hraib *et al.*, 2022)].**

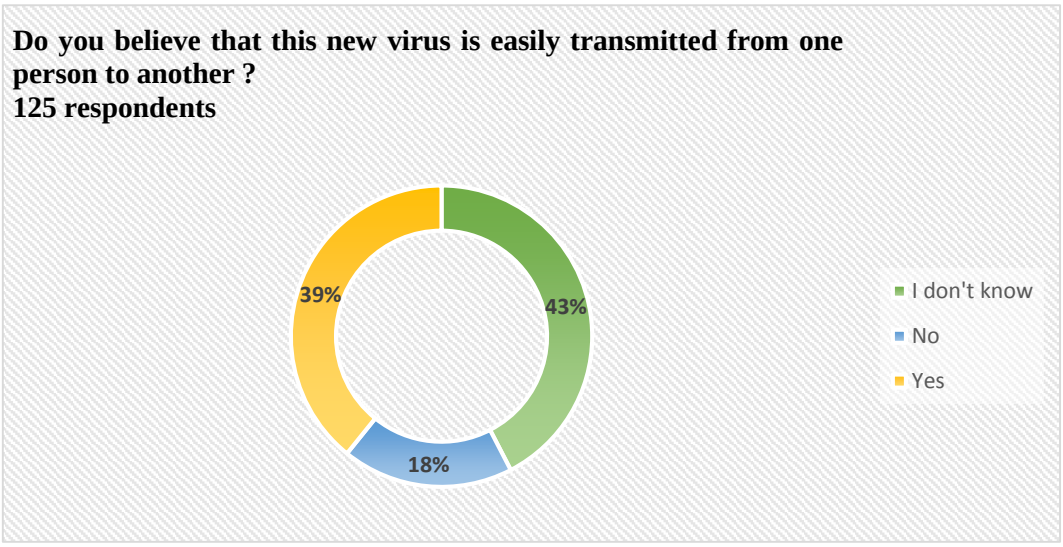


Figure 17: Distribution according to knowledge about the rapid transmission of this virus from person to person.

2.2.7 Distribution according to the factors that contributed to MPXV emergence

According to the participants, there are several factors that promote their emergence and a large part of them (32.2%) consider that the decrease in vaccine protection against smallpox is the first responsible reason for this phenomenon **(Figure 18).** During the 1970s and 1980s, individuals vaccinated against smallpox showed a lower incidence of infection with MPXV, and only 13% of individuals with Monkeypox had a history of smallpox vaccination **(Ejaz *et al*., 2022).** Besides, it is very important to note that homosexuality plays a major role in the emergence of this virus. The CDC Data suggest that most patients are amongst the homosexual or bisexual men in the current outbreak **(Ajmera *et al*., 2022).**

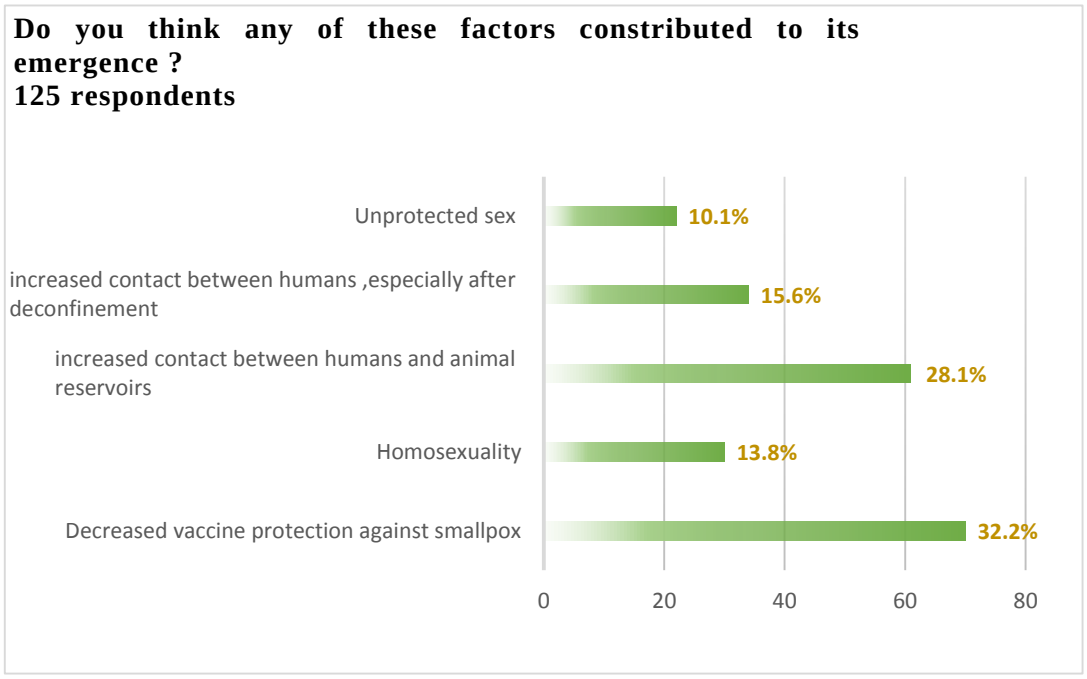


Figure 18: Distribution according to the factors which contributed to its emergence.

2.2.8 Distribution according to the method of its detection during its appearance in 2022

Through the diagram below **(Figure 19),** the majority of students, teachers and administrative workers chose distinctive symptoms of this disease, the availability of PCR tests especially after COVID-19 and the awareness of the risks of infectious diseases (38%, 30.8%, and 30.2%,respectively) were the major ways that led to its detection in 2022. According to scientists, its infection can be asymptomatic like in the UK outbreak where many cases did not have the typical clinical manifestations of Monkeypox **(Harapan *et al.*, 2022).** Additionally, PCR was considered as the best way to detect this infection but it shows positivity only from 2 days to 20 days (median 5 days) after the onset of clinical symptoms **[(Ejaz *et al.*, 2022) ; (Harapan *et al.*, 2022)].**

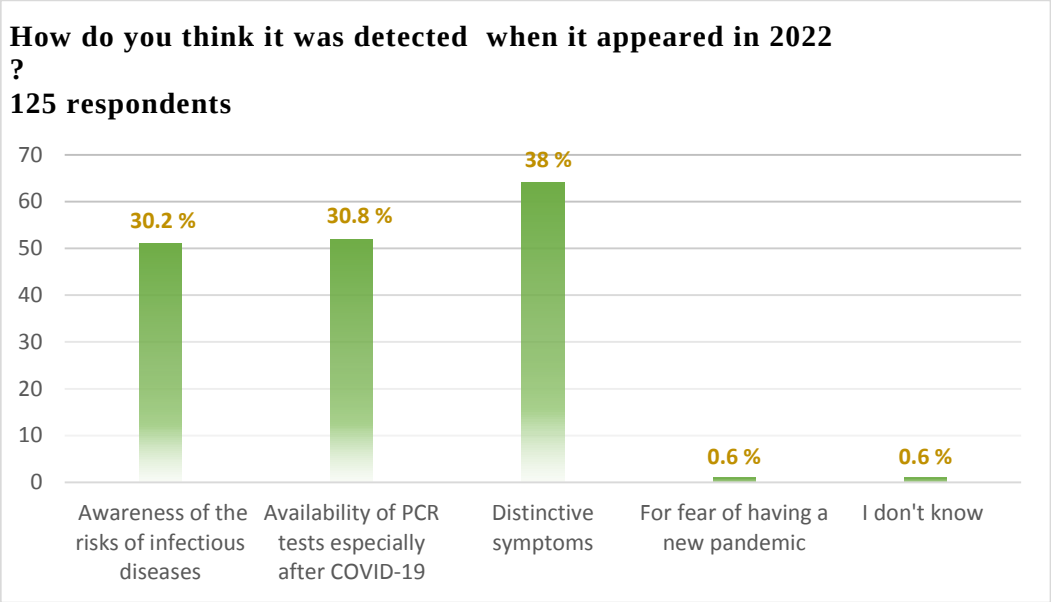


Figure 19: Distribution according to the method of its detection during its appearance in 2022.

2.2.9 Distribution according to the contraction of symptoms associated with this disease

According to **Figure 20,** most of participants have never had any symptoms related to this disease (86%), while according to **Figure 21,** a small group indicated that they had met people with these symptoms (9%).

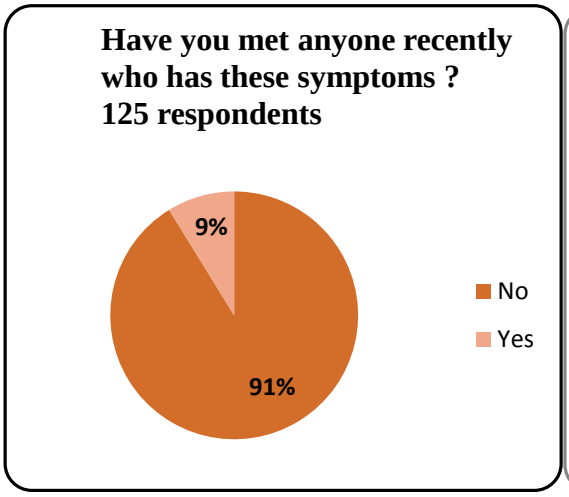


Figure 21: Distribution according to the meeting of someone recently who presents symptoms which associated with this disease.

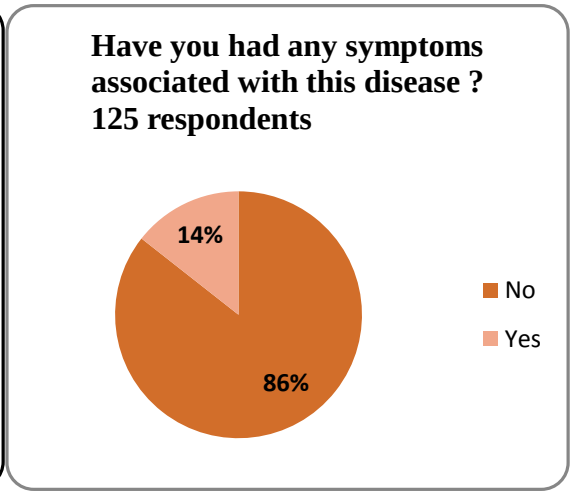


Figure 20: Distribution according to contraction of symptoms associated with this disease.

Among the 24 respondents, they indicated that they may be exposed to this disease by carrying associated symptoms, like fever (39.5%), muscle pain and backache (23.2%), skin eruption (23.2%), and swollen lymph nodes (14%) **(Figure 22).** This might be due to the high similarity between the symptoms of Monkeypox, Smallpox, Measles and Chickenpox which may also explain by the fact that Algeria has not yet recorded any official cases of this virus **[(Altindis *et al.*, 2022) ; (Harapan *et al.*, 2022) ; (Hraib *et al.*, 2022) ; (Titanji *et al.*, 2022)].**

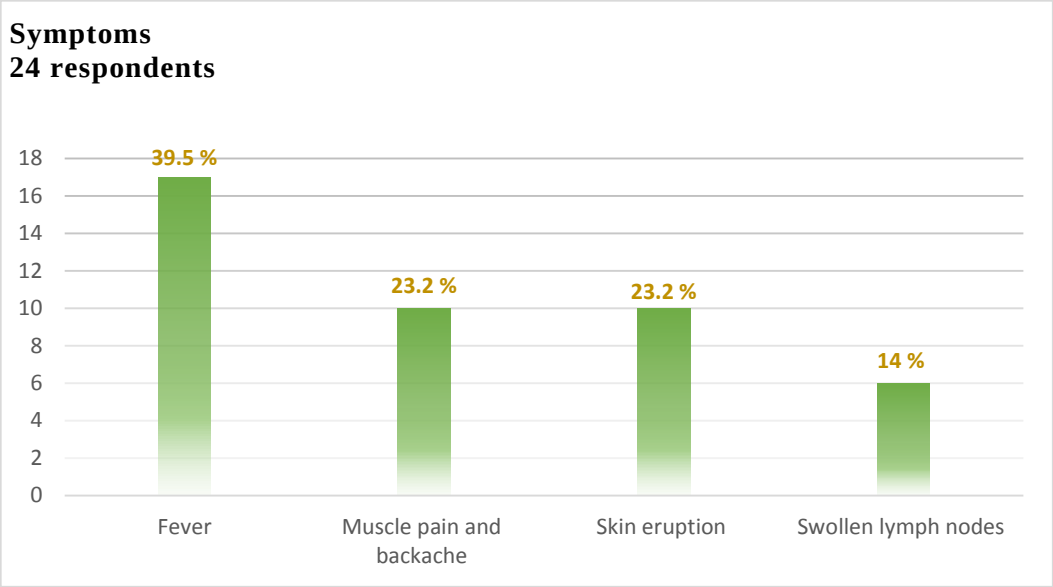


Figure 22: Distribution according to symptoms.

2.2.10. Distribution according to the knowledge of preventive measures recommended to avoid transmission of Smallpox disease.

The results show that 48% of the participants knew the preventive measures to avoid transmission of this disease **(Figure 23).** This result can indicate the consciousness of our participants to follow the news and be updated on the hygienic status concerning emerging viruses in order to avoid repeating the same mistakes made previously in the COVID-19 pandemic era.

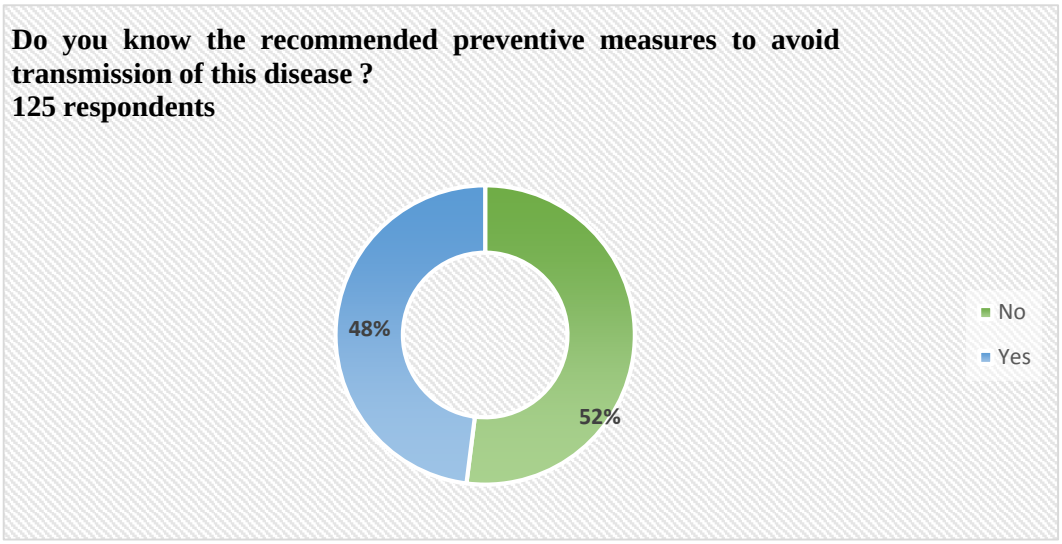


Figure 23: Distribution according to the knowledge of preventive measures recommended avoiding transmission of this disease.

According to different studies, there are many preventive measures that can be considered to avoid MPX infection including, avoiding direct contact with animals that are suspected of harboring MPXV, especially in geographical locations where Monkeypox disease is prevalent, to avoid contact with any material that has been in contact with a sick animal or human **(Kumar *et al.*, 2022),** and to maintain a distance of at least 1 meter from suspected individuals, as well as wearing a well-fitted mask and disposable gloves around them **(Ophinni *et al.*, 2022)**. Furthermore, cooking all foods containing animal meat or components thoroughly **(Upadhayay *et al.*, 2022).** On top of that, those with suspected or confirmed MPV infection should isolate themselves at home or at another location covering all lesions, wear a mask around others, wash or disinfect their hands after touching lesions, and not share any personal items **(Pastula & Tyler, 2022).**

In this study, 71 participants have declared that the best ways to prevent the transmission of this virus were to avoid contact with infected animals and sick people, wash hands frequently with soap and avoid illegitimate sexual relations (29.5%, 22.8%, and 15.7%, respectively) **(Figure 24).** Moreover, in a previous study in Jordan, the majority of the respondents agree that good hand hygiene is the best way to prevent this emerging virus **(Al Mse`adeen *et al.*, 2023).**

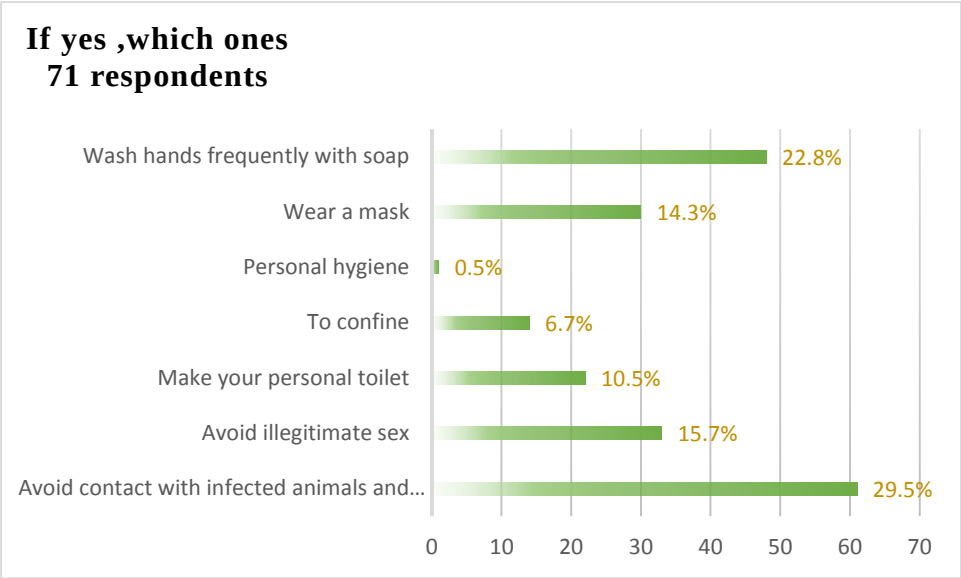


Figure 24: Distribution according to different preventive measures.

2.2.11 Distribution according to the knowledge of the therapeutic and preventive means against the disease of the Monkeypox

According to this diagram **(Figure 25),** 77.3% of the participants knew the therapeutic and preventive means against this disease, and most of them considered that a vaccine is the best way to prevent and treat this disease with 33.3%, followed by antiviral drugs (21.7%).

To date, there are no specialized vaccines and antiviral drugs available for MPXV, although other previous vaccines for small Chickenpox viruses, Cidofovir, ST-246, and VIG can be used to control the Monkeypox epidemics **(Farasani, 2022).** There are categories of people who are more concerned by this treatments including, those whom are suffering from serious diseases such as hemorrhagic diseases, confluent lesions, sepsis, encephalitis, or other diseases requiring hospitalization, also, the immunocompromised population, the pediatric population, especially those under 8 years old, without forgetting pregnant or breastfeeding women, those with a history of allergic dermatitis, and individuals with other active exfoliative skin diseases, in addition to those with one or more complications like, secondary bacterial skin infection, bronchopneumonia, concurrent diseases, or other co morbidities **(Luo & Han, 2022)**.

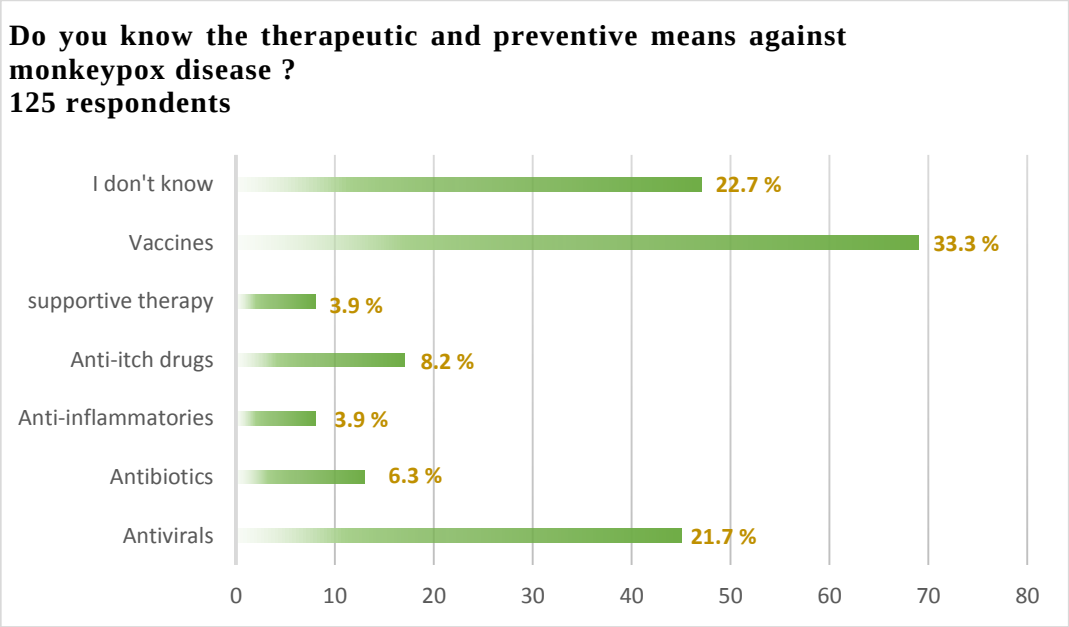


Figure 25: Distribution according to the knowledge of the therapeutic and preventive means against the disease of the Monkeypox.

2.2.12 Distribution according to the knowledge of countries that have launched vaccination against this emerging virus

Through the results that we obtained; the majority of the participants (73.6%) did not know if there were countries that started vaccinating their citizens against this infectious disease **(Figure 26).** It should be noted that the UK and US were the first countries to pursue vaccination to close contacts of MPX cases and Spain became the first European Union country to receive delivery of Monkeypox vaccines, afterwards, more and more countries have decided to offer vaccination to people exposed to MPXV or at risk of acquiring it, like Canada **[(Aljabali *et al*., 2022) ; (Kupferschmidt, 2022) ; (Kmiec & Kirchhoff, 2022)]**.

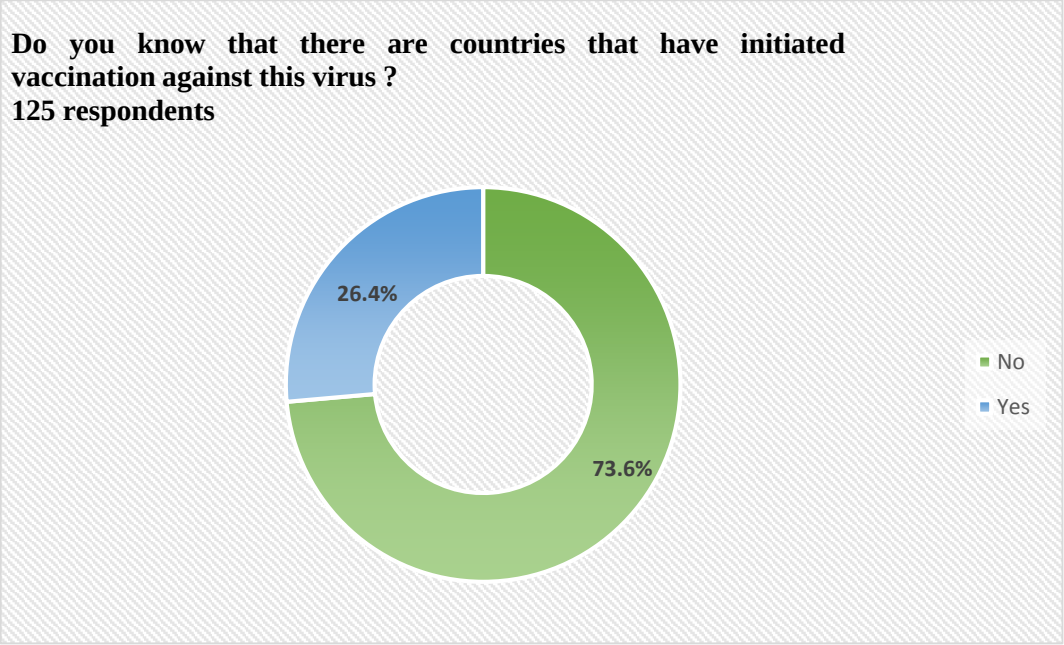


Figure 26: Distribution according to the knowledge of the countries that have launched vaccination against this emerging virus.

2.2.13 Distribution according to the reasons of marketing the vaccines

Through the Figure below **(Figure 27),** we note that more than half of the participants (52%) did not give their opinion about the real reason for marketing these vaccines. In the other half, part of them claimed that it's for the pursuit of financial profit (30.4%), as for the remaining group (26.4%), they believe that these vaccines are marketed due to their benefits and positive results in combating this zoonotic virus. Past evidence does indicate that smallpox vaccines can prevent the spread of MPXV infections due to cross-reaction, with an estimated efficacy of 85% **[(Alakunle e*t al.*, 2020) ; (Sah *et al.*, 2022)].** Moreover, epidemiological investigations indicated that approximately 90% of confirmed MPXV cases had not been infected with other poxviruses (They are not immune to other poxviruses) **(Gong et al., 2022).**

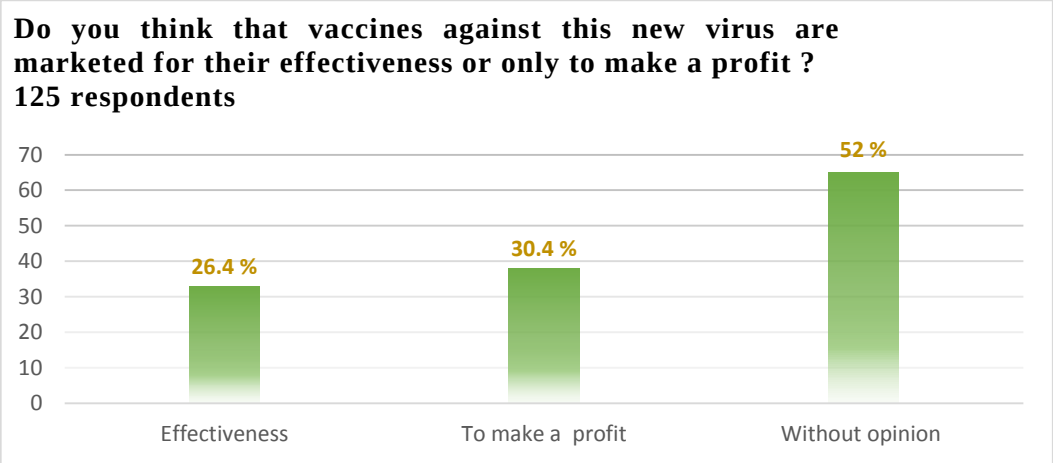


Figure 27: Distribution according to the reasons of marketing the vaccines.

2.2.14 Distribution according to the existence of similarities between infection by the Monkeypox virus and infection by the SARS-COV-2 virus.

Among all of our participants, 58% indicate that there are no similarities between the two infections, while the rest of them (42%) do distinguish that, there are some common ones **(Figure 28).** By comparing many studies, we notice that there are some similarities between the two infections in terms of methods of transmission, as both can be transmitted to people through close, direct contact, with infected person's secretions and droplets, or in terms of the preventive measures that must be taken in order to limit their spread **[(Zatla *et al.*, 2021a) ; (Zatla *et al.*, 2021b) ; (Kaler *et al.*, 2022)],** also as both of them share some common symptoms, like, fever, headache and vomiting **[(Banerjee *et al.*, 2020) ; (Ranganath *et al.*, 2022)].** But we also notice some differences between the two of them like the incubation period which is between 5 and 15 days for SARS-COV-2 virus and between 5 to 3 weeks for Monkeypox virus, further, the difference in terms of the key symptom, like the classic rash of Monkeypox and ARDS (Severe Acute Respiratory Syndrome for COVID-19 **[(Chen, 2020) ; (Zatla *et al.*, 2022) ; (Ajmera *et al.*, 2022)]**.

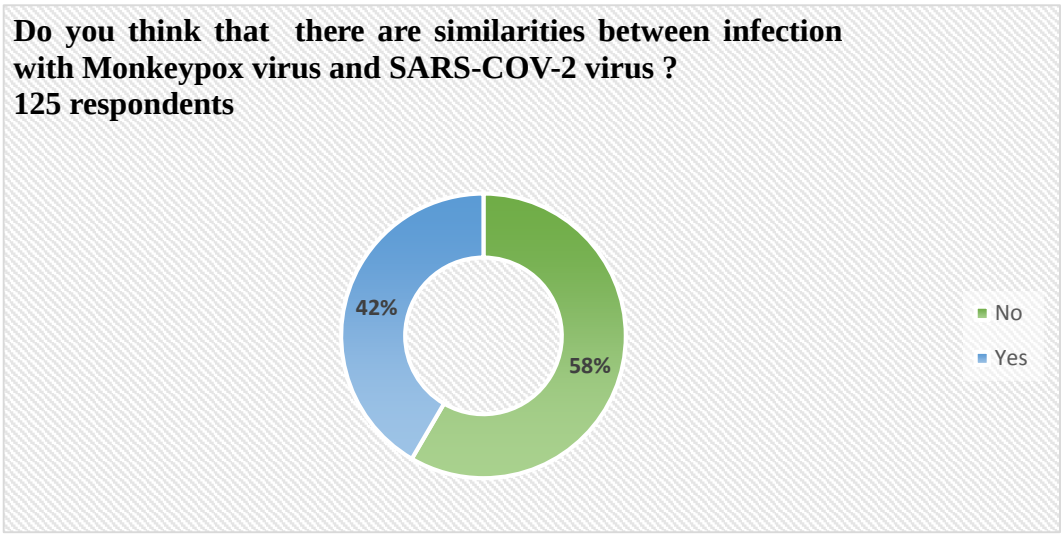


Figure 28: Distribution according to the existence of similarities between infection by the Monkeypox virus and infection by the SARS-COV-2 virus.

2.2.15 Distribution according to the risk of having a new pandemic such as that of SARS-CoV-2

Our data shows that 52% of participants think that there is a risk of having a new pandemic like the one of SARS-COV-2 **(Figure 29).** However, the WHO director stated that the infectivity of MPXV is relatively low and this virus may not become a pandemic. Despite these allegations, MPX outbreak has become endemic in more than 20 countries since May 2022 **(Gong *et al.*, 2022)**. Adding to that, the difficulty to eradicate this virus since it remerges and exists in a multiple animal reservoirs **(Weinstein *et al.*, 2005).** For that every moment there is a possibility and risk of exposure to this new pandemic.

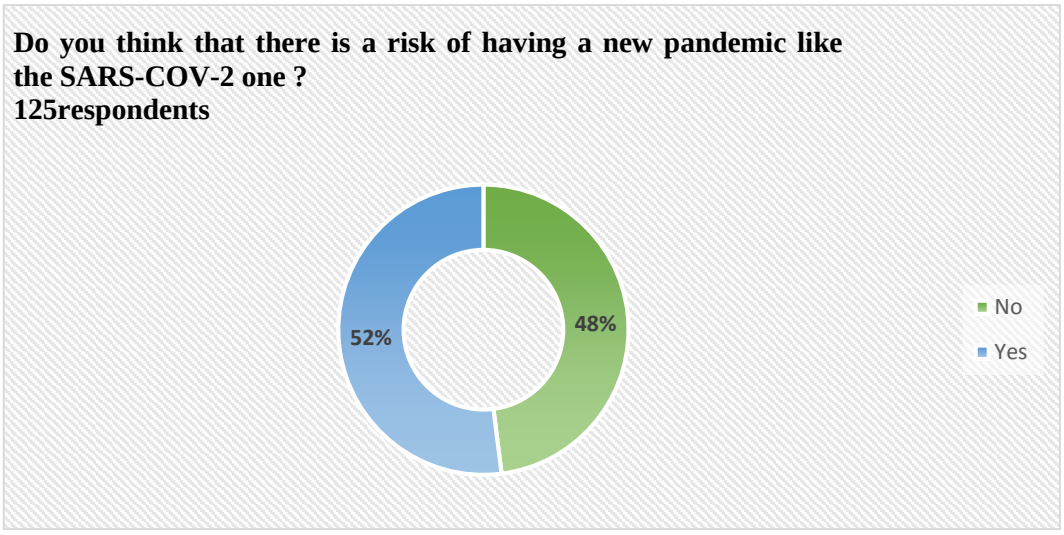
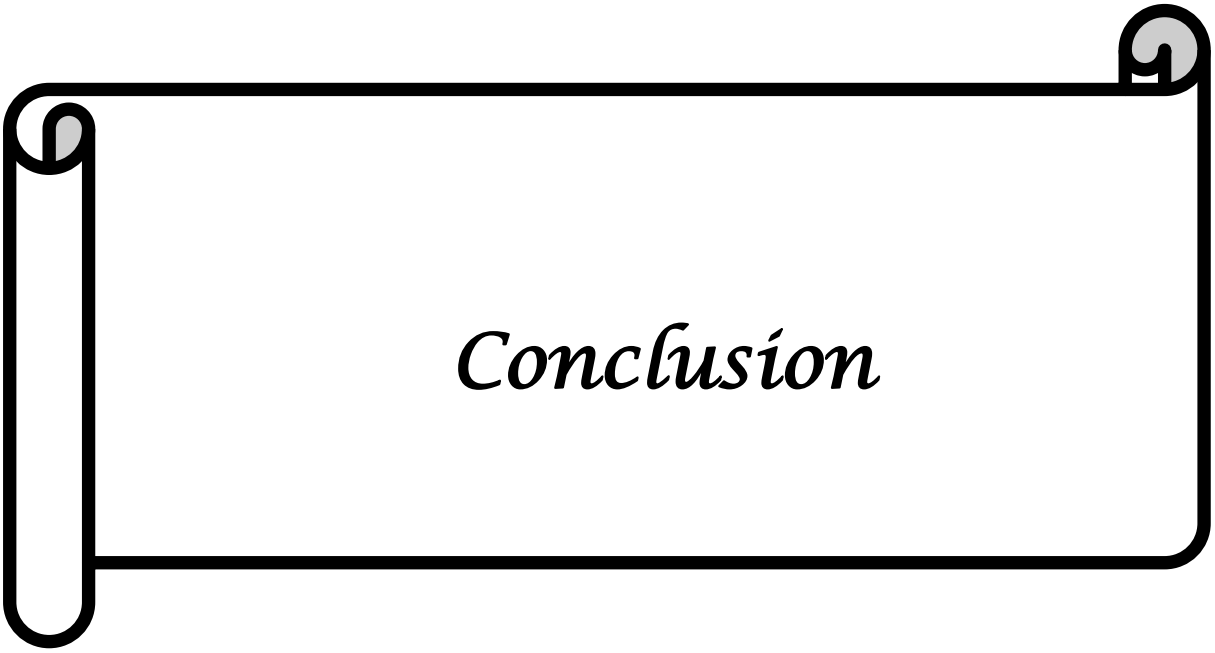


Figure 29: Distribution according to the risk of having a new pandemic such as that of SARS-CoV-2.


Conclusion

After 42 years of eradication of the smallpox disease; a skin disease which is regarded as an ancient and one of the most lethal disease that affects humans, the fight has begun again for the eradication of the MPXV which is considered as a highly uncommon and contagious Orthopoxvirus that is currently a challenge throughout the globe **[(Davenport *et al*., 2018) ; (Chakraborty *et al*., 2022)],** causing many outbreaks, primarily among men that are identified as homosexuals or bisexuals **[(Abed Alah et al., 2022) ; (Guarner *et al*., 2022)].**

The rapid spread of this emerging virus and its disease has once again highlighted the need for rigorous studies to focus on epidemiology, transmission patterns and understand which clade is more infectious than other during the current spread of infections by determining the role of animal reservoirs, and genetic mutations of this virus **[(El Eid *et al*., 2022) ; (Chakraborty *et al*., 2022)].** At the same time, it's very important to understand the true extent of all the symptoms of Monkeypox and its long-term effects **(Kaler *et al*., 2022).** Moreover, one can only control this disease by good hygiene practices, avoid unsafe sexual intercourse ,and more importantly, to vaccinate **(Kumar *et al*., 2022).**

In our study which aimed to evaluate knowledge of Teachers, Administrative-Workers and Students of the Faculty of Natural and Life Sciences and Earth and Universe Sciences of University of Tlemcen about Monkeypox virus in order to spread awareness about the disease and its transmission for anticipating any outbreak in Algeria, we found that our participants had a satisfactory level of knowledge for the mode of transmission, and the preventives measures to fight against the spread of this emerging virus. Furthermore, most of the participants showed a positive attitude towards vaccines, considering them as the best therapeutic means to combat the spread of MPX disease.

Although there are still many unanswered questions about Monkeypox disease, animal reservoirs, and the virus itself, through this humble work we tried to answer and clarify some important points that all people should know about emerging viruses in general and Monkeypox virus and its disease in particular, in order to prepare in advance for any outbreaks in Algeria.

By the end, to stand against this virus in one hand, we urge scientists, doctors and policymakers to assemble and form the proper strategies to contain the recent spread of the virus, and on the other hand, we ask people not to repeat the mistakes made in the COVID-19

pandemic era by being more aware, self-conscious, and also not to get carried away by fake news and rumors.

A question that remains in our minds is what would be the future of these emerging viruses? & would the scenario of COVID-19 pandemic ever be repeated?

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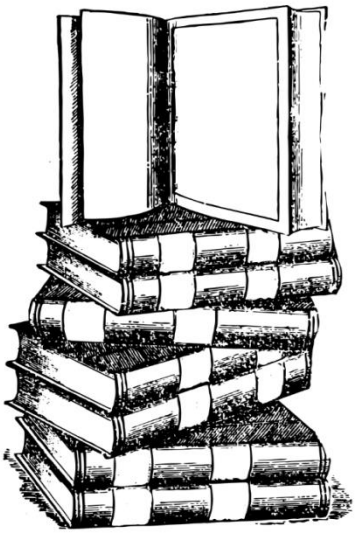

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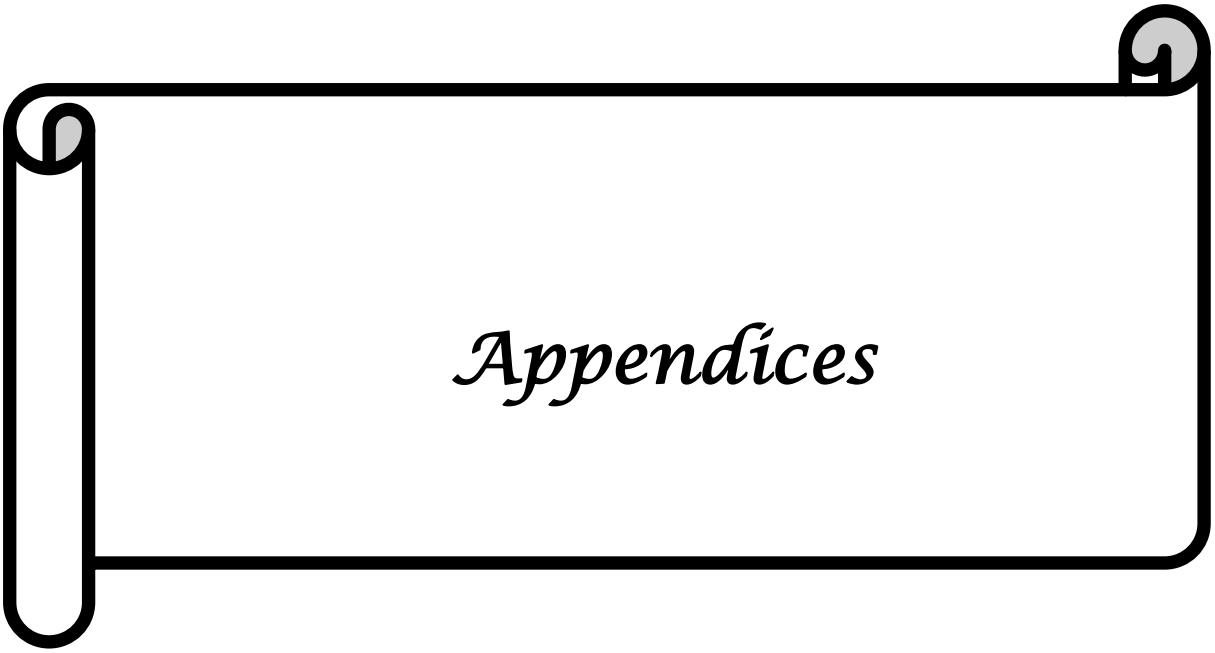
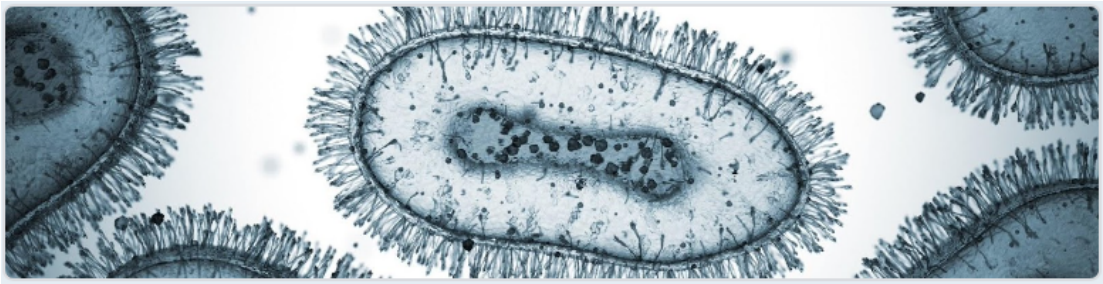

Appendices

Appendice 1



Rubrique 1 sur 2

Etat de connaissance sur la variole et le nouveau virus de la variole de singe (Monkeypox) au niveau de la faculté SNV/STU de l'Université de Tlemcen

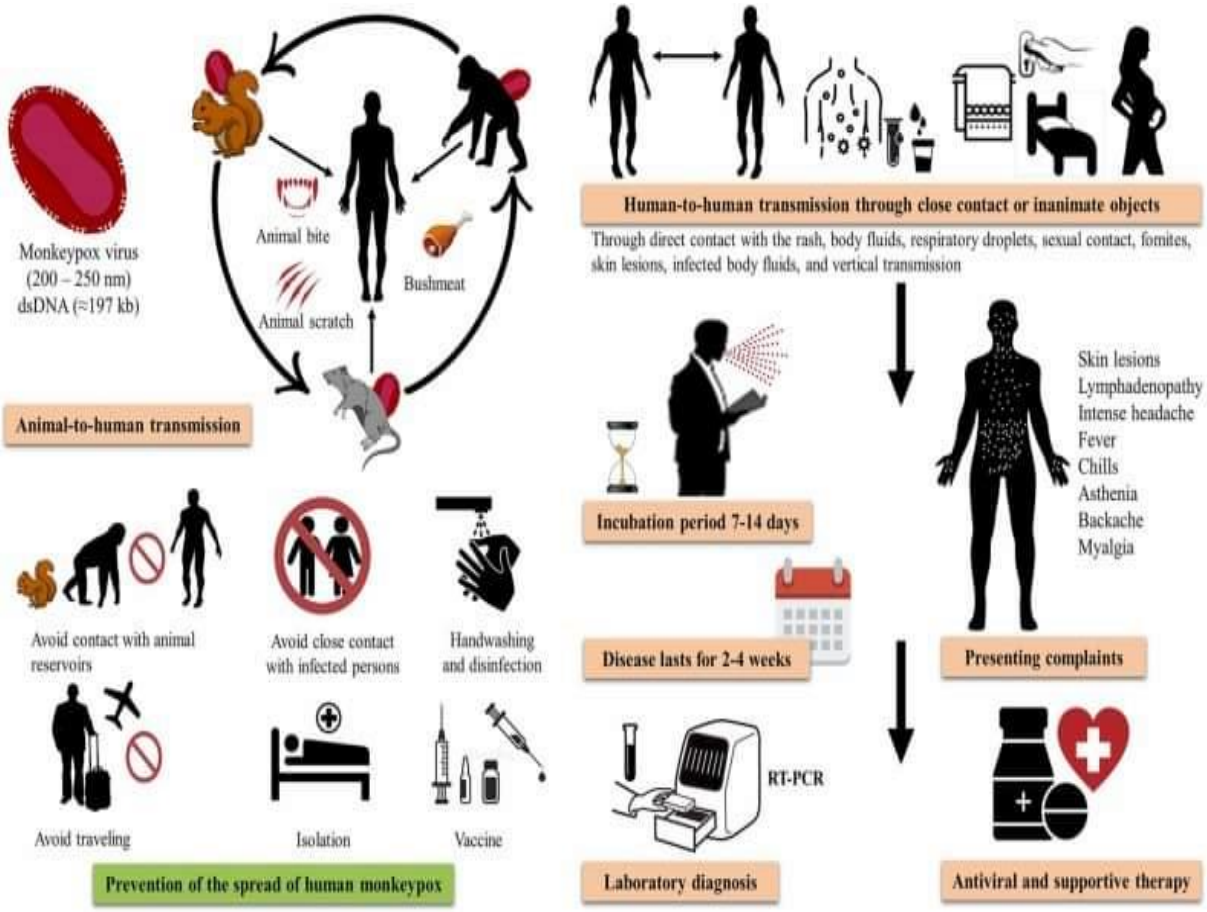
La variole est une maladie causée par le virus du monkeypox (MPXV). Il s'agit d'une infection zoonotique virale identifiée pour la première fois dans des colonies de singes gardées pour la recherche en 1958, et elle n'a été détectée que plus tard chez l'homme en 1970.
Jusqu'en 2021, l'infection à MPXV était essentiellement une pathologie d'Afrique de l'Ouest et d'Afrique Centrale, et exceptionnelle hors Afrique, mais ces données ont brutalement évolué à partir de Mai 2022, après que le premier cas a été détecté à Londres chez un patient ayant récemment voyagé depuis le Nigeria. Des cas autochtones d'infection à MPXV ont été rapportés en Angleterre, puis dans différents pays d'Europe qui étaient jusque-là non endémiques pour cette pathologie infectieuse.

Ce questionnaire servira à récolter des données pour la réalisation d'un mémoire de fin d'études qui a pour objectif de mettre le point sur l'état de connaissances concernant le nouveau virus de Monkeypox, au niveau de la faculté des sciences de la nature et de la vie, sciences de la terre et de l'univers de l'Université de Tlemcen.

Encadrant: Dr. Lamia Boublenza / lamia.boublenza@univ-tlemcen.dz
Co-encadrant: M. Ilyes Zatla / ilyes.zatla@univ-tlemcen.dz
Masterante: Mlle. Wafa Abid / wafa.abid@univ-tlemcen.dz

NB/ Si vous répondez à ce questionnaire , vous consentez à ce que vos réponses soient incluses dans cette recherche, sous couvert anonymat.

Appendice 2


Monkeypox virus
(200 – 250 nm)
dsDNA (≈197 kb)
Animal bite
Bushmeat
Animal scratch
Animal-to-human transmission
Avoid contact with animal reservoirs
Avoid close contact with infected persons
Handwashing and disinfection
Avoid traveling
Isolation
Vaccine
Prevention of the spread of human monkeypox
Human-to-human transmission through close contact or inanimate objects
Through direct contact with the rash, body fluids, respiratory droplets, sexual contact, fomites, skin lesions, infected body fluids, and vertical transmission
Incubation period 7-14 days
Disease lasts for 2-4 weeks
RT-PCR
Laboratory diagnosis
Skin lesions
Lymphadenopathy
Intense headache
Fever
Chills
Asthenia
Backache
Myalgia
Presenting complaints
Antiviral and supportive therapy

ملخص

بينما العالم كله مشغول ومضطرب بشأن كيفية الخروج من وباء SARS-CoV-2 بأقل ضرر ممكن، ظهر فيروس جديد ناشئ اسمه Monkeypox واستحوذ على كل الاهتمام من خلال تصدره جميع الأخبار، مع نشر الذعر بين الناس. من خلال تهديد صحتهم، وتوقع سيناريو COVID-19 في أي لحظة، إن لم يكن أسوأ.

لتقييم المعرفة حول هذا الفيروس ومرضه، ولزيادة الوعي بين أعضاء كلية العلوم الطبيعية وعلوم الحياة وعلوم الأرض والكون في جامعة تلمسان، أطلقنا استبيانًا عبر الإنترنت لمدة عشرين يومًا احتوت على أسئلة اجتماعية وديموغرافية وإدراكية حول الفيروس المستجد ومرضه والتحصين.

أظهرت النتائج التي تم الحصول عليها أن غالبية المستجيبين لدراستنا كانوا طلابًا وينتمون إلى قسم علم الأحياء. بالنظر إلى حقيقة أن الجزائر لم تسجل بعد أي حالات إصابة أو تفشي لمرض جدري القرود، فقد أثبت المشاركون مستوى معرفتهم المرضي حول هذا الفيروس المستجد ومرضه. علاوة على ذلك، أظهر معظم المشاركين موقفًا إيجابيًا تجاه اللقاح، معتبرين أنه أفضل وسيلة علاجية لمكافحة مرض MPX. على الرغم من أنMPXV قد لا يصبح وباءً، إلا أن معرفة الطرق المختلفة التي تساهم في انتشاره أمر ضروري لتجنب أي احتمال لانتشار جديد، خاصة في الجزائر.

الكلمات المفتاحية: فيروسات مستجدة، فيروس جدري القردة، مرض جدري القردة ، استبيان، جامعة تلمسان.

Abstract

While the whole world is busy about how to get out of the SARS-CoV-2 pandemic with the least possible damage, a new emerging virus named Monkeypox Virus (MPXV) appeared and captured all the attention by topping all the news, while spreading panic among people by threatening their health, expecting at any moment a COVID-19 scenario, if not worse.

To evaluate knowledge about this virus and its disease, and to raise consciousness among the members of the Faculty of Natural and Life Sciences and Earth and Universe Sciences in the University of Tlemcen, we launched an online web-based survey for a twenty days' period that contained sociodemographic and perceptiveness questions about the emergent virus, its disease, and vaccination.

Results obtained showed that the majority of the respondents of our study was students and belonged to the Department of Biology. In view of the fact that Algeria has not yet recorded any Monkeypox cases and outbreaks, the participants have proven their satisfactory level of knowledge about this emerging virus and its disease. Moreover, most participants showed a positive attitude towards the vaccine, considering it the best preventive means to fight against MPX disease.

Although the MPXV may not become a pandemic, but knowing the various ways that contribute to its spread is essential to avoid any possibility of a new, especially in Algeria.

Keywords: Emerging viruses, Monkeypox virus, Monkeypox disease, Survey, University of Tlemcen.

Résumé

Alors que le monde entier est occupé sur la façon de sortir de la pandémie de SRAS-CoV-2 avec le moins de dégâts possibles, un nouveau virus émergent nommé Monkeypox virus MPXV (La variole du singe) est apparu et a capté toute l'attention en faisant la une de toutes les nouvelles, tout en semant la panique parmi les gens, en menaçant leur santé, s'attendant à tout moment à un scénario COVID-19, sinon pire.

Afin d'évaluer les connaissances sur ce virus et sa maladie, et de sensibiliser les membres de la Faculté des Sciences Naturelles et de la Vie et des Sciences de la Terre et de l'Univers de l'Université de Tlemcen, nous avons lancé une enquête en ligne d'une durée de vingt jours qui contenait des questions sociodémographiques et de connaissance sur le virus émergent, sa maladie et la vaccination.

Les résultats obtenus ont montré que la majorité des répondants de notre étude étaient des étudiants et appartenaient au département de biologie. Compte tenu du fait que l'Algérie n'a pas encore enregistré de cas et d'épidémies de Monkeypox, les participants ont prouvé un niveau satisfaisant de connaissances sur ce virus émergent et sa maladie. De plus, la plupart des participants ont montré une attitude positive envers le vaccin, le considérant comme le meilleur moyen préventif pour lutter contre la maladie MPX.

Bien que le MPXV ne présente pas de risque de devenir, il est crucial de comprendre différentes voies à sa propagation afin de prévenir toute éventualité d'une nouvelle épidémie, notamment en Algérie.

Mots-clés : Virus émergents, Monkeypox virus, Monkeypox disease, Enquête, Université de Tlemcen