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Review Article

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Review on Middle East Respiratory Syndrome Coronavirus disease (MERS-COV) in Dromedary camel and Its public health importance

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Abstract

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) that was first identified in Saudi Arabia in 2012 is caused by a virus of 2C beta Corona virus lineage that expresses the dipeptidyl peptidase 4 (DPP4) receptor and is densely endemic in dromedary camels of East Africa and the Arabian Peninsula. The first case of MERS-CoV was detected from a 60-year-old man from Saudi Arabia, who died of severe respiratory distress and renal failure. The virus spread over 27 countries with high fatality rate of 35.4% making an ongoing public health threat. Extensive works performed on origin of MERS-CoV indicated that, bats are ancestral host due to their huge species variations, long time fly, and unique behavior of multispecies coexistence. Strong evidence of human-to-human transmission was obtained from epidemiological and genomic studies investigating clustering of cases in hospitals and among household contacts. Zoonotic transmission in human results clinical symptoms ranging from mild to severe respiratory symptoms. Similarly, humans can be infected through direct contact with infected camels or their milk, urine or other body fluids. For identification and characterization of the virus, diagnostic methods such as serological tests, molecular methods and neutralizing assays are used. Studies indicated that, MERS-CoV entrenched in the Arabian Peninsula has acquired increased pathogenic potential for humans due to mutation in their spike protein. Although human cases are yet not detected in Africa, if pathogenic clade B viruses from the Arabian Peninsula are introduced into Africa, they are likely to become dominant and increases public health risks. Therefore, the purpose of this review is to highlight MERS-CoV in dromedary camel and its public health importance.

Keywords: Arabian Peninsula; Dromedary Camels; MERS-CoV; Public Health

1. Introduction

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a novel *betacoronaviridae* family that causes a severe respiratory disease with a high case fatality rate. The virus was first isolated in 2012 from 60 years old man, who died of respiratory distress and renal failure. Up to now World Health Organization (WHO) confirmed that the virus affected almost 2578 from 27 countries laboratory-confirmed cases with 888 associated deaths. Majority of the cases (80%), were from Saudi Arabia, where a high incidence of MERS-CoV in dromedary camel has been linked to human infections, due to their direct contact with sick camels (WHO, 2021).

The most probable sources of infection are bats, due to genetic similarity with human genome. However, people have little chance of contact with them directly (Xia *et al*., 2015;Yixuan, 2020). Similarly, dromedary camels are the intermediate reservoirs for its transmission from bat to human, but, the accurate role of transmission in camel is not clear. In the upper respiratory tract of dromedary camels, the virus may multiply efficiently causing symptoms, including nasal and lachrymal discharge, coughing, sneezing, elevated body temperature, and loss of appetite (Adney *et al*., 2014).

The interaction of the virus with the host Dipeptidyl peptidase 4 (DPP4) using spike protein (S) allows the entry of the virus into the host respiratory cells. MERS-CoV infects and replicates in the human airway epithelial cells and suppresses the production of interferons (IFN) (Kindler *et al*., 2013;Chan *et al*., 2013). unlike other coronavirus variants, MERS-CoV exhibits wider tissue tropism (Chan *et al*., 2013). Compared with other corona variants, MERS-CoV induce pro-inflammatory cytokines. This suggests that, MERS-CoV induces delayed pro-inflammatory response and attenuates innate immunity, which made MERS-CoV is more lethal compared with SARS-CoV (Lau *et al*., 2013; Yini and Wunderink, 2018).

Study indicated that, geographically and genetically distinct viruses from Africa have low replication competence in the human lung, providing a possible explanation for the absence of severe MERS disease in Africa (Chu *et al*., 2018). The findings suggest that MERS-CoV escalating in Arabian Peninsula has acquired increased pathogenic potential for humans due to phenotypic different in their spike protein. If pathogenic clade B viruses from the Arabian Peninsula are introduced into Africa, they are likely to become dominant, as they have in the Arabian Peninsula, and to be associated with adverse health impacts in Africa and increased pandemic threat (Zhou *et al*., 2021).

Due to global incidence of a high number of MERS-CoV cases and deaths indicates that the disease must be considered a serious hazard to public health. Similarly, every year, millions of pilgrims from 184 nations travel to Saudi Arabia to undertake the Hajj and Umrah rituals, which are thereafter travel back in many places throughout the world (Lessler *et al*., 2016). There have been several outbreaks of human-to-human MERS-CoV transmission outside Arabian Peninsula and the largest one occurred in South Korea in 2015 (Oh *et al*., 2018;John *et al*, 2020). Further, this outbreak resulted significant morbidity and mortality, as well as economic, social, and health security consequences (Oh *et al*., 2018).

Diagnosis of MERS-CoV is the major concern in the most diagnostic laboratories. It is recommended to screen MERS-CoV using Real-time reverse-transcription polymerase chain reaction (rRT-PCR) of the upstream of envelope gene (upE) followed by confirmation of the presence of one of the following genes; open reading frame (ORF) 1a, 1b genes or nucleocapsid (N) gene. Scientist are looking to implement viral sequencing on all negative samples of rRT-PCR and they believe that can be exposed to another level of testing using sequence of the RNA-dependent RNA Polymerase (RdRp) gene on N gene and in this case a positive result is diagnostic (Johani and Hajeer, 2016). Reusken *et al*., (2014) evaluated the presence of toxoplasmosis and respiratory tract disease including MERS-CoV from 188 samples collected from three different regions in Ethiopia; Somali, Oromia and Afar, and revealed a seropositivity of 93% from adult camels and 97% from young.

The uncertainty of pathogen transmission, lack of vaccine against MERS-CoV and deficit in specific treatments make public health interventions challenging to design (Durai *et al*., 2015). These makes MERS-CoV is a current public health issue with high reproductive number and fatality rate as compared with other members of Corona virus. However, attentions are not given and the available information is not enough. Therefore, the objective of this review is to give highlights on the available information about MERS-CoV in dromedary camel and its public health importance.

2. Literature Review

2. 1. History

Coronaviruses have long been known to infect humans and several animal species, causing systemic infections of respiratory airways, intestine, liver, and nervous system (Weiss and Navas-Martin, 2005). Previously, human Coronaviruses such as HCoV-229E, HCoV-NL63, HCoV-OC43 and HCoVHKU1 were known to cause mild and self-limiting respiratory diseases mainly upper respiratory tract infections in the human population. Nevertheless, three outbreaks due to human Coronaviruses have been already witnessed in the last two decades. The first outbreak caused by SARS-CoV-1 tries around the world leading

to the death of 774 (9.56%) cases out of 8096 reported to the (WHO) (Lam *et al*., 2003).

The causative agent of the second outbreak was identified as MERS-CoV by an Egyptian virologist, he isolated and identified a previously unknown coronavirus from lung of 60 years old Saudi Arabian man who died of pneumonia and acute renal failure in 2012 (Zaki *et al*., 2012). Collaborative efforts were used in the identification of the MERS-CoV, after routine diagnostics failed to identify the causative agent, Zaki contacted Ron Fouchier, a leading virologist at the Erasmus Medical Center (EMC) in Rotterdam, Netherlands, for advice, Fouchier sequenced the virus from a sample and sent back to Zaki (Lau *et al*., 2017).

Foucher used a broad-spectrum pan coronavirus rRT-PCR to look for distinguish feature of a number of known coronaviruses including (OC43, 229R, NL63, and SARS-CoV) as well as RdRp, a gene conserved in all coronaviruses known to infect humans. While the screens for known coronaviruses were all negative, the RdRp screen was positive (Lu and Liu, 2012).

49-year-old Qatari male who had been flow up at London hospital, UK, was diagnosed with severe respiratory sickness caused by a novel strain of Coronavirus and named London1 novel CoV 2012 in September, 2012, and published the virus preliminary phylogenic tree and genetic sequence. it showed that it is closely to bat coronaviruses. Based on the RNA of the virus obtained from the Qatari case on 25 September 2012, WHO announced that it was engaged in further characterizing the novel coronavirus and that, it had immediately been altered all its members states about the virus and has been leading the coordination and providing guidance to health authorities and technical health agencies (HPA, 2012).

After the comparison with the other already available genetic makeup the family including, SARS, and preliminary name, Human Coronavirus-Erasmus Medical Center (HCoV-EMC), Dr. Zaki and co-authors from the EMC revealed more details on the virus genetic makeup, and published in New England Journal of Medicine on November 8, 2012 (Zaki *et al*., 2012). The official designation of MERS-CoV was adopted by WHO in May 2013 by the Corona virus study Group of the International Committee on Taxonomy of Viruses to create uniformity and simplify communication about the disease (WHO, 2013).

2. 2. Etiology

It is well known that multiple Corona viruses are found naturally and their genetic recombination happens with variable characteristics of their extended hosts. The genomic organization and expression pattern are similar in all coronaviruses. Genetic evolution of this virus helps to jump the species barrier and causes severe morbidity and mortality to humankind (Su *et al*., 2020).

Human coronaviruses (HCoVs) belong to the genera *Alphacoronavirus* and *Betacoronaviruses* within the subfamily *Coronaviridae*. MERS-CoV being the most virulent virus of the genus *betacoronaviridae* is further divided into four genetic clades, termed clades A, B, C and D (de Groot *et al*., 2013). It is a single stranded RNA (ssRNA) genome of length ~29Kb encoding replicase polyprotein open Reading Fragments (ORF) 1a and b, spike glycoproteins (S,) membrane proteins(M), envelop protein (E), and the nucleocapsid and five nonstructural proteins coded by ORF 3, 4a, 4b, and 5 (Fig1) (Wang *et al*., 2018).

The ORFs scattered between these genes are the specific site of mutation, deletion and insertion that helps in the evolution of recombinant lethal virus types. (Raj *et al*., 2013) stated that S protein of the MERS-CoV has two domains, S1 and S2 of which S1 helps in the membrane fusion by engaging the DPP4 receptors found in human cell surface associated with immune regulation, signal transduction, and apoptosis (Haagmans *et al*, 2016).Virion enters the host cells with the fusion enabled by the Receptor Binding Domain (RBD) region with the cell receptors, which triggers a cascade of conformational changes leading to the formation of pre-hairpin intermediate of S2 protein. From this pre-hairpin structures the hydrophobic heptad repeat HR1 subunit extends and enables the fusion by inserting the fusion peptide into the host cell membrane. Then this intermediate refolds with HR2 forming six-helix bundle structures that pulls the host cell membrane much closer to the viral envelop enhancing the fusion (Qian *et al*., 2013).

MERS-CoV differs from SARS-CoV in that it employs DPP4 as its receptor rather than angiotensin-converting enzyme 2 (ACE2) (Tanonaka and Marunouchi, 2016). This shows that, unlike SARS-CoV, which underwent substantial mutation to adapt to the human ACE2 protein, MERS-CoV spike protein adaptation to human DPP4 is not occurring (He *et al*., 2004). Genetically and photogenically characterized

camels from different parts of Africa including Ethiopia indicated that phylogenetically distinct from contemporary viruses from the Arabian Peninsula, but remain antigenically similar in microneutralization tests (Chu *et al*., 2018).

MERS-CoV sequences acquired from nasopharyngeal swabs from two infected human cases dwelling on a farm and three seropositive camels on the same farm were found to be identical during one outbreak in Qatar (Haagmans *et al*, 2016). Another case from Jeddah, Saudi Arabia, shared unique single nucleotide polymorphism (SNP) signature was detected in both a MERS CoV patient and a MERS-CoV-carrying dromedary camel. Comparison of the consequence of the full genome of the MER-CoV variant associated with Korean outbreak showed 99.96-99.98% similarity with the full genome of CoVs obtained from a camel in Riyadh, Saudi Arabia (Azhar *et al*., (2014).

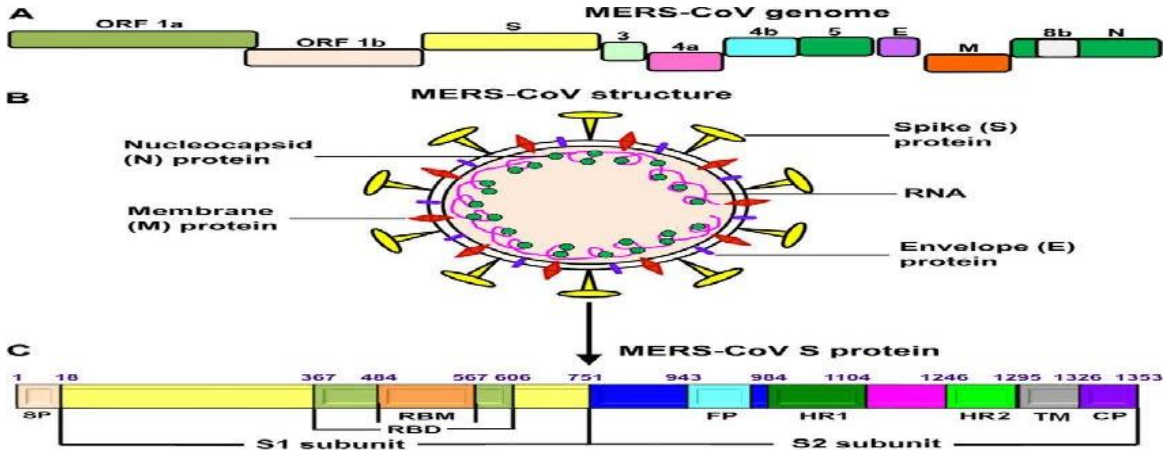

Figure 1: The MERS-CoV genome structure and virion.
Source: (Wang *et al*., 2018).

2.3. Epidemiology

From the time it first appeared in Saudi Arabia in 2012 to the present the virus has infected and spread across more than 27 nations resulting large number of confirmed cases in laboratories. The MERS-CoV outbreak in South Korea in 2015 resulted in 186 cases and 38 deaths. Five super spreaders were responsible for 83% of cases of transmission and 44% of 186 cases were in patients who had nosocomial infection at 16 institutions. The outbreak lasted two months and the government confined 16,993 people for 14 days in order to contain it. So, the outbreak offers a unique chance to close the knowledge gap in MERS-CoV infection (Oh *et al*., 2018).

In 2016, Saudi Arabia reported 1901 confirmed cases with 732 deaths among diverse patients. Further, A total of 13 cases were reported between October to November 2017, amongst which 12 cases were male and only one case was female (WHO, 2017). At December 31, 2018, the laboratory confirmed cases reached 2,279 of MERS-CoV and were recorded from 27 countries in the world, with 806 deaths (Harcourt *et al*., 2018).

According to WHO, (2021), at the end of August, 2021, a total of 2578 laboratory confirmed cases including 888 associated deaths were reported globally The majority of these cases were reported from Saudi Arabia (2178 cases) including 810 related deaths. Epidemiological studies from Lau *et al*., (2017);David *et al*., (2018) revealed human-to-human MERS-CoV transmission is ineffective, and the major infection mechanism is direct/indirect contact with dromedary camels, while other species may possibly serve as reservoirs. On the other hand human clusters of MERS-CoV, have been consistently detected in healthcare, particularly, among persons with chronic illnesses or impaired immunity (Memish *et al*, 2013; Nam *et al*., 2020).

The risk factors for MERS-CoV transmission discovered that recent exposure to dromedary or its raw products, chronic diseases, or close contact with other MERS patients were the main drivers of infection risk (Xia *et a*l., 2015; Alraddadi *et al*., 2016). Further studies revealed that people working closely with camels (e.g., farm workers, slaughterhouse workers, and veterinarians), children, pregnant women, immunocompromised patients, may be at higher risk of MERS-CoV infection than people who do not have regular close contacts with camels (WHO, 2014).

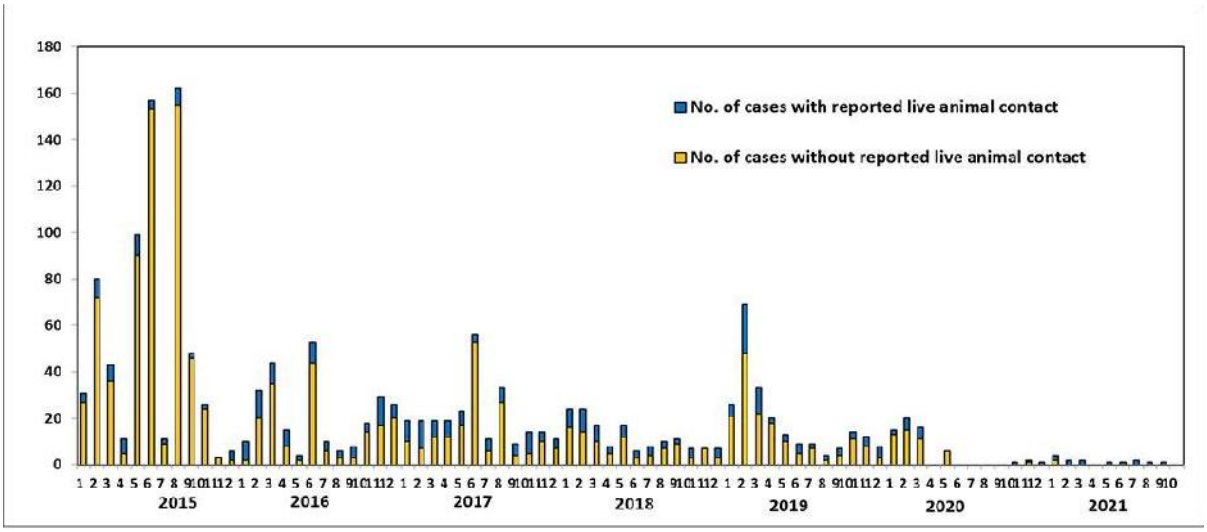

Figure 2: Human epidemiological timeline (with cases reporting animal exposure in blue), by month of disease onset since January 2015.
Source: (WHO, 2021)**.**

2.4. Pathogenesis

Similar to the others human corona virus, MERS-CoV infects and replicates in the airway epithelial cells and suppresses the production of interferons (Kindler *et al*., 2013). However, MERS-CoV exhibit wider tissue tropism This made the virus more pathogenic from the other variant causing higher number of deaths (35.4%) (Chan *et al*., 2013).

Primarily, the entry of the virus into the respiratory tract is facilitated by its type-I transmembrane glycoprotein known as S protein, this interacts with the host Dipeptidyl Peptidase (DPP4). Similarly, the virus enters the cell through an auxiliary pathway on the cell surface via trans-membrane proteases (Weiss and Navas-Martin, 2005).

Coronavirus nonstructural protein 1(nsp1) is a serious virulence factor, which facilitates the biological actions of MERS-CoV. Studying the nsp1 can advances our understanding of pathogenicity of MERS-CoV and facilitate development of better therapeutics. The understanding of MERS-CoV pathogenesis has been limited due to nonavailability of patient autopsy or pathological samples from the patients. Our understanding of the disease pathogenesis is based entirely on *in vitro* studies (Dianna, 2016).

2.5. Transmission

Due to the special features of bats and their huge species variation make them an important ancestral host of various viruses. Similarly, their unique behavior of multiple-species co-existence in a single colony, their long-life span, and their long flying habits across geographical locations, has helped in frequent evolution of recombinant viral pathogens and inter-species transmission (Krishnamoorthy *et al*., 2020;Memish *et al*., 2013).

The RBD in the S protein of the HKU4 bat corona virus is highly similar to that of MERS-CoV and pseudo typed viruses containing the HKU4 S protein can bind human DPP4 and enter cells *in vitro* (Wang *et al*., 2014). HKU4 S protein binds human DPP4 with low affinity, but 2 mutations in the bat S gene, N762A and S746R, allowed HKU4 to bind with higher affinity and enter human cells more efficiently. These changes in the S1/S2 junction in MERS-CoV are part of human proteas emotes, which enhance S protein cleavage and human cell infection, and may have played a role in MERS-CoV transmission from bats to people (Ying *et al*., 2014).

There is increasing evidence that MERS-CoV is spread by dromedary camels. Anti-MERS-CoV antibodies have been found in the sera of dromedary camels from all over the world, particularly in the Middle East and across Africa, including Nigeria,

Tunisia, Egypt, and Ethiopia (Kasem *et al*., 2018). Similarly, serological studies on camels in Africa and the Middle East within the last 30 years suggested that MERS-CoV was circulating among camels for decades before it was first documented in human beings in 2012 (Meyer *et al*., 2016).

MERS-CoV human infection levels in Africa are lower than expected, implying that human infections may be under-reported, possibly due to a lack of testing resources. Extending sero surveys to the general public might help researchers better grasp the scope of MERS-CoV infection in Africa (Handlers *et al*., 2021).

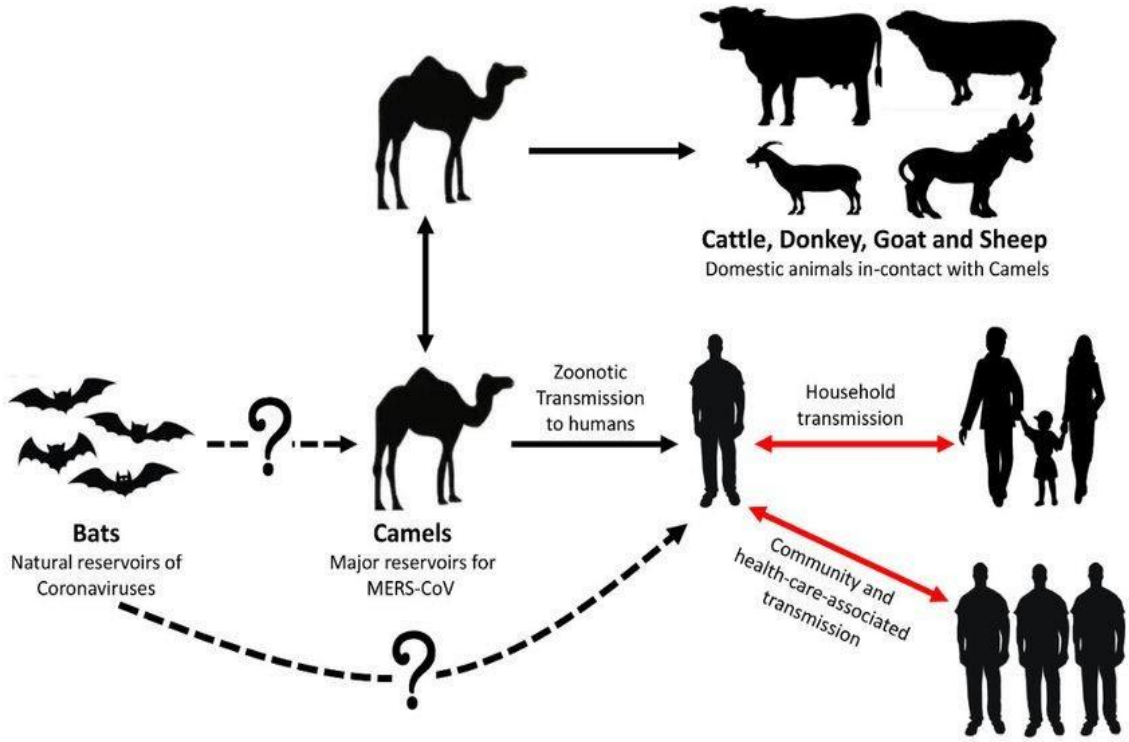

Figure 3: Zoonotic mode of transmission of MERS-CoV.
Source: (Kandeil *et al*., 2019).

2.5.1. Camel-to-Camel Transmission

MERS-CoV RNA is detected most frequently in younger camels (*Alagaili et al., 2014.)* but has been detected in camels >4 years of age (Khalafalla *et al*., 2015). In a longitudinal study of a camel dairy herd, most calves became infected with MERS-CoV at 5–6 months of age, around the time maternal MERS-CoV antibodies wane. The calves then produced MERS-CoV antibodies by 11–12 months of age (Wernery *et al*., 2014). In seroprevalence studies, camels <2 years of age demonstrated lower seroprevalence than camels >2 years of age (Meyer *et al*., 2016) Across many countries, the seroprevalence of adult camels is >90% (Sikkema *et al*, 2019).

Overall, these data suggest most camels are initially infected with MERS-CoV at <2 years of age. However, camels can shed virus despite preexisting MERS-CoV antibodies, suggesting that repeat infections are possible (Van Doremalen *et al*., 2017). Varying prevalence of MERS-CoV RNA in camels has been reported in different countries and settings, such as farms (Khudhair *et al*., 2019) and live animal markets (Haagmans *et al*., 2016). Risk for camel-to-camel or camel-to-human transmission may be influenced by crowding, mixing of camels from multiple sources, transportation, and characteristics of live animal markets (Yusof *et al*., 2017). Phylogenetic modeling has provided supportive evidence that long-term MERS-CoV evolution has occurred exclusively in camels, with humans acting as a transient and usually terminal host (Fèvre *et al*., 2006).

2.5.2. Camel to human transmission

MERS-CoV is a zoonotic virus (passed between animals and humans). It is believed that humans can be infected through direct contact with infected dromedary camels in the Middle East or their milk, urine or other body fluids. (Memish *et al.,* 2013). There is growing evidence that the dromedary camel is a host species for the MERS-CoV and that camels play an important role in the transmission to humans (Hemida *et al.,* 2013). The first evidence of the implication of dromedary camels in transmission was the detection of high rates of MERS-CoV antibodies in dromedary camels on the Arabian Peninsula. Evidence of infection in camels precedes the first evidence of human infection (Haagmans *et al.,* 2014). The detection of MERS-CoV in dromedary camels imported from Sudan and Ethiopia for slaughter in Egypt, as well as serological evidence of previous MERS-CoV infection in dromedaries in Ethiopia, Kenya, Nigeria, Tunisia and the Canary Islands (Spain; some originating from Morocco) suggests that the virus could be geographically widespread in the dromedary camel populations on the African continent and that previously undetected transmission to humans may occur outside of the Arabian Peninsula (Corman *et al.,* 2014).

2.5.3.Human-to-Human Transmission

Strong evidence of human-to-human transmission was obtained from epidemiological and genomic studies investigating clustering of cases in hospitals and among household contacts (Müller *et al.,* 2015). Human-to-human transmission of MERS-CoV can occur, but humans are considered transient or terminal hosts (Fèvre *et al.,* 2006) with no evidence for sustained human-to-human community transmission.

Therefore, human-to-human transmission was also responsible for most of the MERS-CoV cases reported during the outbreak that occurred in Jeddah in 2014 (Oboho *et al.,* 2015). The majority of cases were attributable to contact with a health care facility, other patients, or both, highlighting the role of healthcare facilities in human-to-human transmission that also arose in subsequent outbreaks, including hospital outbreaks in Riyadh and the 2015 outbreak in Korea (Balkhy *et al.,* 2016).

Healthcare facility human-to-human transmission has been associated with defective or inadequate infection prevention and control measures coronavirus infections (Cotton *et al.,* 2014). The infection tends to be milder in secondary cases, in which a patient is infected as a result of close contact with a primary source, and can even be asymptomatic. The number of cases who get infected from confirmed cases is low; the rate of transmission among household contacts has been calculated to be around 5% in one study done in Kingdom of Saudi Arabia (KSA)in 2014 (Memish *et al.,* 2014). However, epidemiological analysis of the Korean hospital outbreak in 2015 showed that the fatality rate was not significantly different between primary cases and subsequent generations (Kim, 2015). This outbreak highlighted the danger posed by a combination of circumstances including a primary source traveling from the Middle East, infection among secondary and tertiary contacts due to movement of infected individuals between healthcare facilities, and inadequate infection prevention and control measures (Nishiura *et al.,* 2016).

2.6. Clinical Features

The clinical presentation caused by MERS-CoV has an average incubation time of 5 days (4-12 in range). In this time the host show no symptoms of infection. The disease started off as a basic respiratory condition, with minor fever, chills, muscle aches, and respiratory stress (shortness of breath) to severe ones such as pneumonitis, as well as respiratory failure in Human (Guery *et al*., 2020).

On admission, patients' laboratory results revealed leukopenia, lymphopenia, thrombocytopenia, and high lactate dehydrogenase levels MERS-CoV can potentially induce severe pneumonia and acute respiratory diseases, which necessitates the use of mechanical ventilation and hospitalization to an intensive care unit. In contrast to the human cases, camel showed minor clinical signs of the disease, including of rhinorrhea and a mild increase in body temperature but no other clinical signs were observed (Drosten *et al*., 2007).

2.7. Diagnosis

Detecting the virus in respiratory tract samples remains the gold standard in diagnosing MERS-CoV infection. Several samples can be obtained from the respiratory system that can be used for diagnosing MERS-CoV infection. These include tracheal aspirates, nasopharyngeal swabs, bronchoalveolar.

Diagnosis of MERS-CoV still a major concern in most of diagnostic laboratories. The confirmation of a probable or suspicious cases can only be accomplished through laboratory testing. Samples should be collected by trained personnel and in consideration of all biosafety instructions and the personal protective equipment (PPE) appropriate for respiratory viruses, according to the WHO guidelines for infection control and bio-risk management (Corman *et al*., 2012).

2.7.1. Serological Testing

ELISA, IFA and Neutralization assays are used to confirm the diagnosis in serology. Based on the isolated S receptor binding region, an in-house Anti-MERS-COV IgM, ELISA kit was created. This extremely sensitive and specific ELISA has previously been verified with camel and human samples (Kapoor *et al*., 2014). Camel samples were analyzed at a 1:20 dilution with goat anti-camel IgM-horseradish peroxidase conjugate as the secondary anti body at 1:3000 based on a microneutralization test with a cut-off vale of 0.35. The secondary anti body was anti-human IgM-horseradish peroxidase conjugate, which was evaluated at a dilution of 1:20 in human plasma (Zohaib *et al*., 2018).

2.7.2. Molecular techniques

MERS-CoV infection is presently diagnosed by molecular testing, which involves detecting viral RNA in clinical samples using rRT-PCR assays. A positive rRT-PCR for two particular genomic targets or a single positive target with a second target sequenced. A sample from the upper respiratory system (nasopharyngeal swab) as well as a sample from the lower respiratory system are required. Because of the increased virus load in lower respiratory samples, they yield more. Serial PCR testing of the URT and LRT, as well as other body compartments (e.g., serum, urine, and feces), is advised to further our understanding of viral replication (Kindler *et al*., 2013).

2.8. Treatment

The treatment of MERS-CoV infected human airway epithelium cultures with IFN of type I or type III has been found to efficiently reduce viral replication. This finding supports the recommendation of IFN as a promising treatment for MERS-CoV (Alagaili *et al*., 2014). Similarly, IFN-1βb with mycophenolic acid was also found to be a successful combination that possessed antiviral activity against MERS-CoV (Chan *et al*., 2013). Furthermore, using of repurposing of drugs, convalescent, monoclonal antibodies, peptides as antiviral therapeutic agents have shown some results (Cao *et al*., 2015).

Convalescent plasma therapy utilizes plasma or whole blood from people who have been infected with viral diseases and recovered. This therapy has been used during outbreaks when no particular medicines or vaccines are available for treatment (Arabi *et al*., 2015). Further, the use of convalescent plasma has been indicated to be an efficient therapeutic strategy for diseases like MERS-CoV (Chong *et al*., 2015).

Therapeutics based on monoclonal antibodies have been used successfully in the therapy of various diseases (Jan ter Meulen *et al*, 2004). The potential of this approach was acknowledged against coronaviruses during the SARS-CoV outbreak (Du *et al*., 2013). Initial studies suggested that MERS-CoV RBD domain in S1 glycoprotein represents a suitable target for the development of neutralizing monoclonal antibodies (Adedeji and Sarafianos, 2014;Ying *et al*., 2014).

Interest has been given in the development of peptide therapeutics as potential drug targets for different pathogens. As compared with chemical drugs, peptide drugs show high specificity toward the target as well as little side effect and drug tolerance (Chong *et al*., 2015). As compared with chemical drugs, peptide drugs show high specificity toward the target as well as little side effect and drug tolerance (Choudhry *et al*., 2019). The antimicrobial peptides block the receptors present on the host cell's surface, which in turn inhibit different steps of viral fusion and replication causing virolysis and activation of host's adaptive immune response (Zumla *et al*., 2016).

2.9. Prevention and Control

Although there are three vaccines in development (one to prevent transmission from camels to people, and two for use in humans during outbreaks and longer-term protection of people at high risk), currently no vaccine available for the prevention of MERS-CoV in humans or camels. Therefore, Understanding the route and pattern of MERS-CoV transmission is critical for effective control and prevention. People who are at risk of contracting MERS-CoV should avoid coming into contact with camels, practice proper hand hygiene, and avoid drinking raw milk or eating

contaminated food until it has been adequately washed, peeled, or cooked, according to (WHO, 2014).

2.9.1. One Health-based interventions to stop MERS-CoV disease

Despite current implementation of rapid diagnostic and public health measures, new MERS-CoV cases are still continuously being reported. This suggests that multiple interventions targeting different affected groups would be necessary to stop these disease, as summarized in figure 4 (Maged Gomaa Hemida, 2019)

This may be achieved in many ways including reducing contacts between different hosts, regular monitoring of the population of dromedary camels. Active animal shedders need to be identified, and quarantine measures should apply until they stop shedding the virus. Reorganization and reshaping of the camel industry include allocating the camel markets away from the cities. Global awareness concerning the necessity of thorough boiling and cooking of the camel milk and meat products, respectively, should take place. Animal abattoirs should be established far away from large cities. Thorough decontamination of animals' biological wastes in abattoirs should occur using the appropriate standard protocols. People who are in close contact with the camels should wear proper personal protective equipment at all times (Maged Gomaa Hemida, 2019).

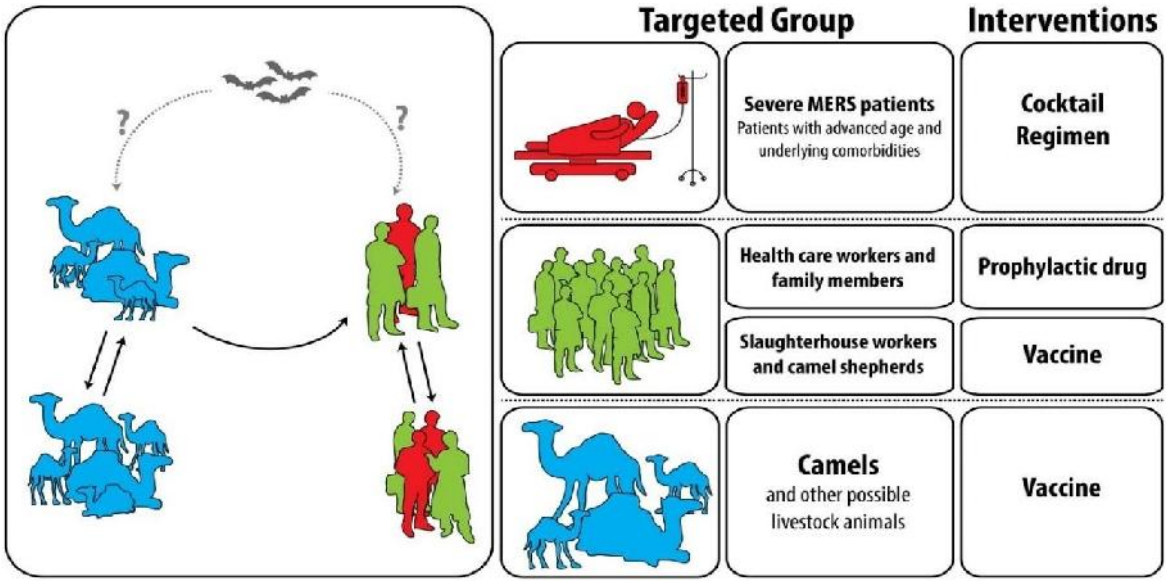

Figure 4: Some interventions based on the One Health approaches to stop MERS-CoV outbreaks.
Source: (Widagdo *et al*., 2017)**.**

2.9.2. Current progress on the control of MERS-CoV

Interestingly, among the affected population, case fatality rate of MERS-CoV dropped from almost 50% in 2012 to 35.4% in 2021, therefore, we relate this progress in the control of MERS-CoV over the past 7 years to many factors (WHO, 2021).

First, identification of the main reservoir of the virus, namely, the dromedary camel (Hemida *et al*., 2014). Second, continuous molecular and serological surveillance of MERS-CoV among the dromedary camel population in the Arabian Peninsula and Africa (Corman *et al*., 2014). Third, vaccination of dromedary camels, especially animals under two years of age, will have a great impact on the reduction of the viral shedding from these animals to the surrounding community (Chan *et al*., 2014). Fouth, new strategies have been adopted to reduce the spread of infection in health care units (Rajakaruna *et al*., 2017). Fifth, some therapeutic and control approaches for MERS-CoV such as cyclosporine, ribavirin and interferon show promising trends for the treatment of MERS-CoV-infected patients (De Wilde *et al*., 2013;Kindler *et al*., 2013). Meanwhile, good progress has been made in screening large numbers of drugs/therapies for the treatment of MERS-CoV (Lau *et al*, 2017). This may lead to the development of some effective novel drugs against MERS-CoV infection in the near future.

3. MERS-CoV in Ethiopia

MERS-CoV has been circulating in African dromedaries for more than 35 years and the seropositive rate in dromedary camels is quite high in the Middle East and in Northern and Eastern African countries. Despite widespread seropositivity for reported in dromedary camels, the human MERS-CoV cases have been observed only in the Middle East (Chu *et al*., 2018).

In Ethiopia, dromedary camels represent a subset of major livestock resources with a population estimated at 1, 209, 321. The pastoralist and agro-pastoralist areas of Ethiopia such as Borena, Bale, Afar and Somali are considered the traditional source of livestock, supplying 95% of camels for export markets and camel is their source of income in terms of food and economic (Teklewold, 2008).

Several studies that focus on viral and serological detection of MERS-CoV in camels were done in some part of the country, but not representative of all camels' population. Recent research finding on MERS-CoV in Ethiopian camels revealed that MERS-CoV in East Africa including Ethiopia is genetically distinct from those in the Arabian Peninsula that strengthens the absence of local acquired zoonotic cases in human (Getnet *et al*., 2017).

A study conducted at Oromia and Afar regional states indicated higher overall prevalence of 93% and 91% respectively (Getnet *et al*., 2017). Similar serological study with the aim of detection and molecular characterization of MERS-CoV was conducted from Somali region (Warder with 100% prevalence), and Oromia region (Babile, Metehara, Ginir, and Moyale and found 49.7% overall prevalence) of Ethiopia. In this study revealed that high prevalence in adult camel compared to the young. However, RT-PCR at National Animal Health and Diagnostic and Investigation center (NAHDIC) showed negative MERS-CoV upE genome from the swab sample (Muluneh, 2021). This doesn't prove the absence of the virus, so further molecular diagnostic techniques, will help the country.

Table 1: Seroprevalence of MERS-CoV in Ethiopia.

Authors	Year	No. of camels	Seroprevalence		RNA prevalence (%)	Stratification
			%	Range %		
(Reusken *et al*., 2014)	2010-11	188	96	95-100	-	Region
(Miguel *et al*., 2017)	2015	632	96	85-99	10	Region
(Dighe *et al*., 2019)	2013	66	96	-	N/A	-

3.1. Phenotypic Characterization of Ethiopian Camel MERS-CoV

Phylogenetically, three clades A, B, and C of MERS-CoVs are recognized (Dianna *et al*, 2016). The earliest MERS-CoV (human/EMC/2012) (EMC) designated as clade A is no longer detectable in humans or in dromedaries. Clade B viruses emerged to become dominant in dromedaries in the Arabian Peninsula, spilling over to cause sporadic zoonotic disease, sometimes leading to clusters of transmission between humans. Viruses detected in camels in East (Egypt, Ethiopia, Sudan, Djibouti, and Kenya), North (Morocco), and West (Nigeria and Burkina Faso) Africa all belonged to different sublineages of clade C (Chu *et al*., 2018).

Preliminary studies comparing the replication competence of human (clade A) and camel (clade B) MERS-CoV from Saudi Arabia with a clade C virus from Burkina Faso, West Africa, showed that the West African viruses had lower replication competence in Calu-3 cells, in ex vivo cultures of human bronchus and lung, and in lungs of hDPP4-transduced mice (Dianna *et al*, 2016) . These West African clade C1.1 viruses had deletions in ORF4b (fig.4) that may contribute to the reduced virus replication competence. It was not known whether viruses from other regions of Africa, such as Ethiopia, where ORF4b deletions are not always found, also share this phenotype of reduced replication in human respiratory cells. Importantly, the highest density of dromedary camels in the world is found in East Africa, which is also the source of export of camels into the Arabian Peninsula. Thus, a more extensive and systematic phenotypic comparison of MERS-CoV from different sublineages and regions of Africa (especially East Africa) with viruses from the Arabian Peninsula is urgently needed.

From the scale bar below indicates the pairwise nucleotide substitutions per site. Taxa labeled with blue and red represent MERS-CoV sequences from human and camels, respectively. ORF3 and ORF4b deletions in the virus genomes are indicated as green and purple boxes, respectively. The virus from Egypt (C270) had no deletions, while the viruses from Ethiopia (CAC9690) and Kenya (CAC10200) characterized in this study (Zhou *et al*., 2021) had no deletion in ORF4 but had a 12-nucleotide deletion in ORF3. Except for the prototype human virus EMC, all camel viruses used in this study were isolated from swab specimens from dromedary camels in

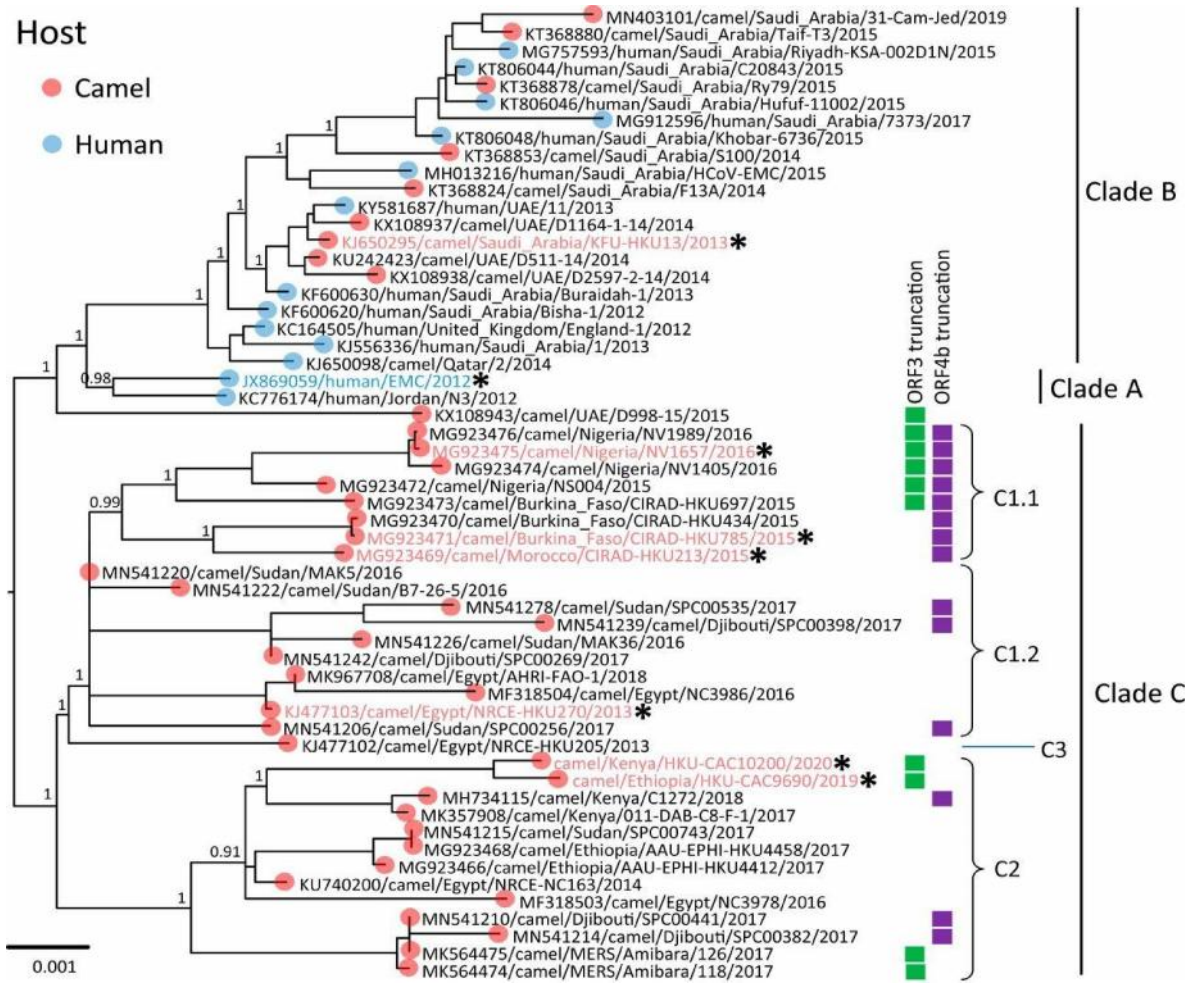

Figure 5: Phylogenetic relationships of the clade A, B, and C MERS-CoVs.
Source: (Zhou *et al*., 2021)**.**

4. Conclusion and Recommendations

MERS is a disease caused by MERS-CoV and was first detected from Saudi Arabia in 2012 by an Egyptian virologist from a 60 years old man. Bats are thought to be ancestral host, due to their interspecies mixing and they play an important role in the transmission of the infection, whereas camel act as intermediate host which poses public health risk to human. Morbidity and mortality rates were found to be increasing with each evolution inferring the fact that genetic variations are more complex with each evolution, improving the pathogenicity of the virus. The current available diagnostic options are Molecular and Serological methods which are showing some promising results. As a means of prevention and control, the only available option is understanding the route and pattern of MERS-CoV transmission. Studies indicated that the virus is more prevalent in African and if pathogenic clade B viruses from the Arabian Peninsula are introduced into Africa, they are likely to become dominant and increases public health risks.

Based on the above conclusive remarks, the following recommendations are forwarded:

- Advances technologies, vaccine platforms, clinical trial designs, and bioinformatics which are supporting MERS-CoV vaccine development should be employed.
- Appropriate follow of international trade guidelines such as food safety standard is needed in order to minimize the spread of the disease.
- Priorities should be given on MERS research, surveillance, management, and control through establishing One Health global approach.
- Direct or indirect contacts between bats, camels and human should be minimized.
- Awareness should be created about the public health aspect of the disease

5. References

Adedeji, A. O., and Sarafianos, S. G. (2014). Antiviral drugs specific for coronaviruses in preclinical development. *Current Opinion in Viroogy* ,**8**:45–53. https://doi.org/10.1016/j.coviro.2014.06.002

Adney, D. R., van Doremalen, N., Brown, V. R., Bushmaker, T., Scott, D., de Wit, E., Bowen, R. A., and Munster, V. J. (2014). Replication and shedding of MERS-CoV in upper respiratory tract of inoculated dromedary camels. *Emerging Infectious Diseases*, **20**(12), 1999–2005. https://doi.org/10.3201/eid2012.141280

Alagaili, A. N., Briese, T., Mishra, N., Kapoor, V., Sameroff, S. C., de Wit, E., Munster, V. J., Hensley, L. E., Zalmout, I. S., Kapoor, A., Epstein, J. H., Karesh, W. B., Daszak, P., Mohammed, O. B., and lan Lipkin, W. (2014). Middle east respiratory syndrome coronavirus infection in dromedary camels in Saudi Arabia. *MBio*, **5**(2), 1–6. https://doi.org/10.1128/mBio.00884-14

Alraddadi, B. M., Watson, J. T., Almarashi, A., Abedi, G. R., Turkistani, A., Sadran, M., Housa, A., Almazroa, M. A., Alraihan, N., Banjar, A., Albalawi, E., Alhindi, H., Choudhry, A. J., Meiman, J. G., Paczkowski, M., Curns, A., Mounts, A., Feikin, D. R., Marano, N., Madani, T. A. (2016). Risk factors for primary middle east respiratory syndrome coronavirus illness in humans, Saudi Arabia, 2014. *Emerging Infectious Diseases*, **22**(1), 49–55. https://doi.org/10.3201/eid2201.151340

Arabi, Y., Balkhy, H., Hajeer, A. H., Bouchama, A., Hayden, F. G., Al-Omari, A., Al-Hameed, F. M., Taha, Y., Shindo, N., Whitehead, J., Merson, L., AlJohani, S., Al-Khairy, K., Carson, G., Luke, T. C., Hensley, L., Al-Dawood, A., Al-Qahtani, S., Modjarrad, K., … Fowler, R. (2015). Feasibility, safety, clinical, and laboratory effects of convalescent plasma therapy for patients with Middle East respiratory syndrome coronavirus infection: a study protocol. *SpringerPlus*, **4**(1), 1–8. https://doi.org/10.1186/s40064-015-1490-9

Azhar, E. I., El-Kafrawy, S. A., Farraj, S. A., Hassan, A. M., Al-Saeed, M. S., Hashem, A. M., and Madani, T. A. (2014). Evidence for Camel-to-Human Transmission of MERS Coronavirus. *New England Journal of Medicine*, **370**(26), 2 499–2505. https://doi.org/10.1056/nejmoa1401505

Cao, J., Forrest, J. C., and Zhang, X. (2015). A screen of the NIH Clinical Collection small molecule library identifies potential anti-coronavirus drugs. *Antiviral Research*, **114**:1–10.

Chan, J. F. W., Chan, K. H., Choi, G. K. Y., To, K. K. W., Tse, H., Cai, J. P., Yeung, M. L., Cheng, V. C. C., Chen, H., Che, X. Y., Lau, S. K. P., Woo, P. C. Y., and Yuen, K. Y. (2013). Differential cell line susceptibility to the emerging novel human betacoronavirus 2c EMC/2012: Implications for disease pathogenesis and clinical manifestation. *Journal of Infectious Diseases*, **207**(11), 1743–1752. https://doi.org/10.1093/infdis/jit123

Chan, R. W. Y., Hemida, M. G., Kayali, G., Chu, D. K. W., Poon, L. L. M., Alnaeem, A., Ali, M. A., Tao, K. P., Ng, H. Y., Chan, M. C. W., Guan, Y., Nicholls, J. M., and Peiris, J. S. M. (2014). Tropism and replication of Middle East respiratory syndrome coronavirus from dromedary camels in the human respiratory tract: An in-vitro and ex-vivo study. *The Lancet Respiratory Medicine*, **2**(10), 813–822. https://doi.org/10.1016/S2213-2600(14)70158-4

Chong, Y. P., Song, J. Y., Seo, Y. Bin, Choi, J. P., Shin, H. S., Yoon, H. J., Choi, J. Y., Kim, T. H., Choi, Y. H., Kim, H. Bin, Yoon, J. H., Lee, J., Eom, J. S., Lee, S. O., Oh, W. S., Cheong, H. J., Song, Y. G., Choi, J. H., and Kim, W. J. (2015). Antiviral treatment guidelines for middle east respiratory syndrome. *Infection and Chemotherapy*, **47**(3), 212–222. https://doi.org/10.3947/ic.2015.47.3.212

Choudhry, H., Bakhrebah, M. A., Abdulaal, W. H., Zamzami, M. A., Baothman, O. A., Hassan, M. A., Zeyadi, M., Helmi, N., Alzahrani, F., Ali, A., Zakaria, M. K., Kamal, M. A., Warsi, M. K., Ahmed, F., Rasool, M., and Jamal, M. S. (2019). Middle East respiratory syndrome: Pathogenesis and therapeutic developments. *Future Virology*, **14**(4), 237–246. https://doi.org/10.2217/fvl-2018-0201

Chu, D. K. W., Hui, K. P. Y., Perera, R. A. P. M., Miguel, E., Niemeyer, D., Zhao, J., Channappanavar, R., Dudas, G., Oladipo, J. O., Traoré, A., Fassi-Fihri, O., Ali, A., Demissié, G. F., Muth, D., Chan, M. C. W., Nicholls, J. M., Meyerholz, D. K., Kuranga, S. A., Mamo, G., … Peiris, M. (2018). MERS coronaviruses from camels in Africa exhibit region-dependent genetic diversity. *Proceedings of the National Academy of Sciences of the United States of America*, **115**(12), 3144–3149. https://doi.org/10.1073/pnas.1718769115

Corman, V M, Eckerle, I., Bleicker, T., Zaki, A., Landt, O., Boheemen, S. Van, Gopal, R., and Ballhause, M. (2012). Detection of a novel human coronavirus by real-time reverse-transcription polymerase chain reaction. *Eurosurveillance*, **17**(39), 1–6. https://doi.org/10.2807/ese.17.39.20285-en

Corman, Victor M., Jores, J., Meyer, B., Younan, M., Liljander, A., Said, M. Y., Gluecks, I., Lattwein, E., Bosch, B. J., Drexler, J. F., Bornstein, S., Drosten, C., and Müller, M. A. (2014). Antibodies against MERS coronavirus in dromedary camels, Kenya, 1992-2013. *Emerging Infectious Diseases*, **20**(8), 1319–1322. https://doi.org/10.3201/eid2008.140596

David, D., Rotenberg, D., Khinich, E., Erster, O., Bardenstein, S., Straten, M. Van, Okba, N. M. A., Raj, S. V, Haagmans, B. L., Miculitzki, M., and Davidson, I. (2018). Middle East respiratory syndrome coronavirus speci fi c antibodies in naturally exposed Israeli llamas , alpacas and camels. *One Health*, **5**:65–68. https://doi.org/10.1016/j.onehlt.2018.05.002

de Groot, R. J., Baker, S. C., Baric, R. S., Brown, C. S., Drosten, C., Enjuanes, L., Fouchier, R. A. M., Galiano, M., Gorbalenya, A. E., Memish, Z. A., Perlman, S., Poon, L. L. M., Snijder, E. J., Stephens, G. M., Woo, P. C. Y., Zaki, A. M., Zambon, M., and Ziebuhr, J. (2013). Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Announcement of the Coronavirus Study Group. *Journal of Virology*, **87**(14), 7790–7792. https://doi.org/10.1128/jvi.01244-13

Dianna L. Ng, Farida Al Hosani, y M. Kelly Keating, Susan I. Gerber, z Tara L. Jones, Maureen G. Metcalfe, Suxiang Tong, x Ying Tao, x Negar N. Alami,{k Lia M. Haynes, Mowafaq Ali Mutei, yy Laila Abdel-Wareth, zz Timothy M. Uyeki, xx David L. Swerdl, kk and S. R. Z. (2016). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- research that is available on the COVID-19 resource centre - including this for unrestricted research re-use a. *The American Journal of Pathology*, **186**: 652–658. http://dx.doi.org/10.1016/j.ajpath.2015.10.024

Dighe, A., Jombart, T., Kerkhove, M. D. Van, and Ferguson, N. (2019). A systematic review of MERS-CoV seroprevalence and RNA prevalence in dromedary camels : Implications for animal vaccination. *Epidemics*, **29**:100350. https://doi.org/10.1016/j.epidem.2019.100350

Drosten, C., Günther, S., Preiser, W., Werf, S. Van Der, Brodt, H., Becker, S., Rabenau, H., Panning, M., Kolesnikova, L., Fouchier, R. M., Drosten, C., Günther, S., Preiser, W., Werf, S. Van Der, Brodt, H., Drosten, C., Günther, S., and Preiser, W. (2007). *Identification of a novel coronavirus in patients with severe acute respiratory syndrome . To cite this version : HAL Id : pasteur-00167033 Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome*.

Du, L., Kou, Z., Ma, C., Tao, X., Wang, L., Zhao, G., Chen, Y., Yu, F., Tseng, C. T. K., Zhou, Y., and Jiang, S. (2013). A truncated receptor-binding domain of MERS-CoV spike protein potently inhibits MERS-CoV infection and induces strong neutralizing antibody responses: Implication for developing therapeutics and vaccines. *PLoS ONE*, **8**(12), 2–10. https://doi.org/10.1371/journal.pone.0081587

Durai, P., Batool, M., Shah, M., and Choi, S. (2015). Middle East respiratory syndrome coronavirus: transmission, virology and therapeutic targeting to aid in outbreak control. *Experimental and Molecular Medicine*, **47**: e181. https://doi.org/10.1038/emm.2015.76

Getnet, F., Gelagay, A., and Fufa, A. (2017). Epidemiological investigation of Middle East respiratory syndrome corona virus (mers-cov) among dromedary camels in selected areas of Afar and Oromia region, Ethiopia. *Journal of Veterinary Medicine and Animal Health*, **9**(3), 47–54. https://doi.org/10.5897/jvmah2015.0454

Guery, B., Poissy, J., Mansouf, L., Séjourné, C., Ettahar, N., Lemaire, X., Vuotto, F., Goff, A., and Behillil, S. (2020). *Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- research that is available on the COVID-19 resource centre - including this for unrestricted research re-use a. January*.

Haagmans, Bart 1 Judith M. A. van den Brand, 1 V. Stalin Raj, 1 Asisa Volz, 2 Peter Wohlsein, 3 Saskia L. Smits, 1 Debby Schipper, 1 Theo M. Bestebroer, 1 Nisreen Okba, 1 Robert Fux, 2 Albert Bensaid, 4 David Solanes Foz, 4 Thijs Kuiken, 1 Wolfgang Ba, 8. (2016). Re s ear ch | r e p o r t s. *Research*, **351**(6268), 77–82.

Handlers, C., Munyua, P. M., Ngere, I., Hunsperger, E., Kochi, A., Amoth, P., Mwasi, L., Tong, S., Mwatondo, A., Thornburg, N., Widdowson, M., and Njenga, M. K. (2021). *Low-Level Middle East Respiratory Syndrome Coronavirus*. **27**(4), 1201–1205.

Harcourt, J. L., Rudoler, N., Tamin, A., Leshem, E., Rasis, M., Giladi, M., and Haynes, L. M. (2018). The prevalence of Middle East respiratory syndrome coronavirus (MERS-CoV) antibodies in dromedary camels in Israel. *Zoonoses and Public Health*, **65**(6), 749–754. https://doi.org/10.1111/zph.12482

He, J. F., Peng, G. W., Min, J., Yu, D. W., Liang, W. J., Zhang, S. Y., Xu, R. H., Zheng, H. Y., Wu, X. W., Xu, J., Wang, Z. H., Fang, L., Zhang, X., Li, H., Yan, X. G., Lu, J. H., Hu, Z. H., Huang, J. C., Wan, Z. Y., … Lo, Y. M. D. (2004). Molecular Evolution of the SARS Coronavirus, during the Course of the SARS Epidemic in China. *Science*, **303**(5664), 1666–1669. https://doi.org/10.1126/science.1092002

Hemida, Maged G., Chu, D. K. W., Poon, L. L. M., Perera, R. A. P. M., Alhammadi, M. A., Ng, H. Y., Siu, L. Y., Guan, Y., Alnaeem, A., and Peiris, M. (2014). Mers coronavirus in dromedary camel herd, Saudi Arabia. *Emerging Infectious Diseases*, **20**(7), 1231–1234. https://doi.org/10.3201/eid2007.140571

Hemida, Maged Gomaa. (2019). Middle East Respiratory Syndrome Coronavirus and the One Health concept. *Peer Journal*, **201**(8). https://doi.org/10.7717/peerj.7556

HPA. (2012). novel coronavirus infection identified in family cluster. *Infection Report*, *8*(1317138119464), 2011–2013. www.hpa.org.uk/webw%0A/HPAwebandHPAwebStandard/HPAweb_C/1317138119464.

Jan ter Meulen, Alexander B H Bakker, Edward N van den Brink, Gerrit J Weverling, Byron E E Martina, Bart L Haagmans, Thijs Kuiken, John de Kruif, Wolfgang Preiser, Willy Spaan, Hans R Gelderblom, Jaap Goudsmit, A. D. M. E. O. (2004). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19. The COVID-19 resource centre is hosted on Elsevier Connect, the company' s public news and

information. *Lancet*, **363**(9427), 2139–41. Crossref. PubMed.

Johani, S. Al, and Hajeer, A. H. (2016). MERS-CoV diagnosis : An update. *Journal of Infection and Public Health*, **9**(3), 216–219. https://doi.org/10.1016/j.jiph.2016.04.005

John C. Smulian Sonja A. Rasmussen MD, M. S. (2020). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-. *Ann Oncol*, **1**:19–21.

Kandeil, A., Gomaa, M., Shehata, M., El-Taweel, A., Kayed, A. E., Abiadh, A., Jrijer, J., Moatasim, Y., Kutkat, O., Bagato, O., Mahmoud, S., Mostafa, A., El-Shesheny, R., Perera, R. A. P. M., Ko, R. L. W., Hassan, N., Elsokary, B., Allal, L., Saad, A., … Kayali, G. (2019). Middle East respiratory syndrome coronavirus infection in non-camelid domestic mammals. *Emerging Microbes and Infections*, **8**(1), 103–108. https://doi.org/10.1080/22221751.2018.1560235

Kapoor, M., Pringle, K., Kumar, A., Dearth, S., Liu, L., Lovchik, J., Perez, O., Pontones, P., Richards, S., Yeadon-Fagbohun, J., Breakwell, L., Chea, N., Cohen, N. J., Schneider, E., Erdman, D., Haynes, L., Pallansch, M., Tao, Y., Tong, S., … Feikin, D. R. (2014). Clinical and laboratory findings of the first imported case of middle east respiratory syndrome coronavirus to the United States. *Clinical Infectious Diseases*, **59**(11), 1511–1518. https://doi.org/10.1093/cid/ciu635

Kasem, S., Qasim, I., Al-Hufofi, A., Hashim, O., Alkarar, A., Abu-Obeida, A., Gaafer, A., Elfadil, A., Zaki, A., Al-Romaihi, A., Babekr, N., El-Harby, N., Hussien, R., AL-Sahaf, A., Al-Doweriej, A., Bayoumi, F., Poon, L. L. M., Chu, D. K. W., Peiris, M., and Perera, R. A. P. M. (2018). Cross-sectional study of MERS-CoV-specific RNA and antibodies in animals that have had contact with MERS patients in Saudi Arabia. *Journal of Infection and Public Health*, **11**(3), 331–338. https://doi.org/10.1016/j.jiph.2017.09.022

Kindler, E., Jónsdóttir, H. R., Muth, D., Hamming, O. J., Hartmann, R., Rodriguez, R., Geffers, R., Fouchier, R. A. M., Drosten, C., Müller, M. A., Dijkman, R., and Thiela, V. (2013). Efficient replication of the novel human betacoronavirus EMC on primary human epithelium highlights its zoonotic potential. *MBio*, *4*(1), 1–6. https://doi.org/10.1128/mBio.00611-12

Krishnamoorthy, S., Swain, B., Verma, R. S., and Gunthe, S. S. (2020). SARS-CoV, MERS-CoV, and 2019-nCoV viruses: an overview of origin, evolution, and genetic variations. *Virus Disease*, **31**(4), 411–423. https://doi.org/10.1007/s13337-020-00632-9

L. Haagmans, Bart 1 Judith M. A. van den Brand, 1 V. Stalin Raj, 1 Asisa Volz, 2 Peter Wohlsein, 3 Saskia L. Smits, 1 Debby Schipper, 1 Theo M. Bestebroer, 1 Nisreen Okba, 1 Robert Fux, 2 Albert Bensaid, 4 David Solanes Foz, 4 Thijs Kuiken, 1 Wolfgang Ba, 8. (2016). *Re s ear ch | r e p o r t s*. **351**(6268), 77–82.

Lam, W. K., Zhong, N. S., and Tan, W. C. (2003). Overview on SARS in Asia and the World. *Respirology*, *8*(July), 29–32. https://doi.org/10.1046/j.1440-1843.2003.00516.x

Lau, S. K. P., Lau, C. C. Y., Chan, K., Li, C. P. Y., Chen, H., Jin, D., Chan, J. F. W., Woo, P. C. Y., and Yuen, K. (2013). *Delayed induction of proinflammatory cytokines and suppression of innate antiviral response by the novel Middle East respiratory syndrome coronavirus : implications for pathogenesis and treatment.* 2679–2690. https://doi.org/10.1099/vir.0.055533-0

Lau, S. K. P., Wong, A. C. P., Lau, T. C. K., and Woo, P. C. Y. (2017). Molecular evolution of MERS coronavirus: Dromedaries as a recent intermediate host or long-time animal reservoir? *International Journal of Molecular Sciences*, **18**(10). https://doi.org/10.3390/ijms18102138

Lessler, J., Salje, H., Van Kerkhove, M. D., Ferguson, N. M., Cauchemez, S., Rodriquez-Barraquer, I., Hakeem, R., Jombart, T., Aguas, R., Al-Barrak, A., and Cummings, D. A. T. (2016). Estimating the severity and subclinical burden of middle east respiratory syndrome coronavirus infection in the Kingdom of Saudi Arabia. *American Journal of Epidemiology*, **183**(7), 657–663. https://doi.org/10.1093/aje/kwv452

Lu, G., and Liu, D. (2012). SARS-like virus in the Middle East: A truly bat-related coronavirus causing human diseases. *Protein and Cell*, *3*(11), 803–805. https://doi.org/10.1007/s13238-012-2811-1

Memish, Z. A., Mishra, N., Olival, K. J., Fagbo, S. F., Kapoor, V., Epstein, J. H., AlHakeem, R., Al Asmari, M., Islam, A., Kapoor, A., Briese, T., Daszak, P., Al Rabeeah, A. A., and Lipkin, W. I. (2013). Middle East respiratory syndrome coronavirus in Bats, Saudi Arabia. *Emerging Infectious Diseases*, **19**(11), 1819–1823. https://doi.org/10.3201/eid1911.131172

Meyer, B., Juhasz, J., Barua, R., Das Gupta, A., Hakimuddin, F., Corman, V. M., Müller, M. A., Wernery, U., Drosten, C., and Nagy, P. (2016). Time course of MERS-CoV infection and immunity in dromedary camels. *Emerging Infectious Diseases*, **22**(12), 2171–2173. https://doi.org/10.3201/eid2212.160382

Miguel, E., Chevalier, V., Ayelet, G., Ben Bencheikh, M. N., Boussini, H., Chu, D. K., El Berbri, I., Fassi-Fihri, O., Faye, B., Fekadu, G., Grosbois, V., Ng, B. C., Perera, R. A., So, T., Traore, A., Roger, F., and Peiris, M. (2017). Risk factors for MERS coronavirus infection in dromedary camels in Burkina Faso, Ethiopia, and Morocco, 2015. *Eurosurveillance*, **22**(13). https://doi.org/10.2807/1560-7917.ES.2017. 22.13.30498

Muluneh, A. (2021). *iMedPub Journals A Cross Sectional Study of Middle East Respiratory Syndrome : Coronavirus*. **6**(5), 1–5.

Nam, H., Wan, J., Ki, M., Yeon, M., and Kim, J. (2020). *Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID- 19 . The COVID-19 resource centre is hosted on Elsevier Connect , the company ' s public news and information . January*.

Oh, M. D., Park, W. B., Park, S. W., Choe, P. G., Bang, J. H., Song, K. H., Kim, E. S., Kim, H. Bin, and Kim, N. J. (2018). Middle east respiratory syndrome: What we learned from the 2015 outbreak in the republic of Korea. *Korean Journal of Internal Medicine*, **33**(2), 233–246. https://doi.org/10.3904/kjim.2018.031

Qian, Z., Travanty, E. A., Oko, L., Edeen, K., Berglund, A., Wang, J., Ito, Y., Holmes, K. V, and Mason, R. J. (2013). Innate Immune Response of Human Alveolar Type II Cells Infected with Severe Acute Respiratory Syndrome – Coronavirus. *Am J Respir Cell Mol Biol Vol*, **48**(22), 742–748. https://doi.org/10.1165/rcmb.2012-0339OC

Raj, V. S., Mou, H., Smits, S. L., Dekkers, D. H. W., Müller, M. A., Dijkman, R., Muth, D., Demmers, J. A. A., Zaki, A., Fouchier, R. A. M., Thiel, V., Drosten, C., Rottier, P. J. M., Osterhaus, A. D. M. E., Bosch, B. J., and Haagmans, B. L. (2013). Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature*, **495**(7440), 251–254. https://doi.org/10.1038/nature12005

Rajakaruna, S. J., Liu, W., Ding, Y., and Cao, G. (2017). *Strategy and technology to prevent hospital-acquired infections : Lessons from SARS, Ebola, and MERS in Asia and West Africa*. 1–6. https://doi.org/10.1186/s40779-017-0142-5

Reusken, C. B. E. M., Messadi, L., Feyisa, A., Ularamu, H., Godeke, G. J., Danmarwa, A., Dawo, F., Jemli, M., Melaku, S., Shamaki, D., Woma, Y., Wungak, Y., Gebremedhin, E. Z., Zutt, I., Bosch, B. J., Haagmans, B. L., and Koopmans, M. P. G. (2014). Geographic distribution of MERS coronavirus among dromedary camels, Africa. *Emerging Infectious Diseases*, **20**(8), 1370–1374. https://doi.org/10.3201/eid2008.140590

Su, S., Wong, G., Shi, W., Liu, J., Lai, A. C. K., Zhou, J., Liu, W., Bi, Y., and Gao, G. F. (2020). *Epidemiology , Genetic Recombination , and Pathogenesis of Coronaviruses*. *January*.

Tanonaka, K., and Marunouchi, T. (2016). Angiotensin-converting enzyme 2. *Folia Pharmacologica Japonica*, **147**(2), 120–121. https://doi.org/10.1254/fpj.147.120

Teklewold, H. (2008). *Live animal and meat export value chains for selected areas in Ethiopia : Constraints and opportunities for enhancing meat exports Live animal and meat export value chains for selected areas in Ethiopia : Constraints and opportunities for enhancing meat e*. *January*.

Chan W. Y. AGuan, Y., Poon, L. L. M., Baric, R. S., Nicholls, J. M., and Malik, J. S. (2013). *Tropism of and Innate Immune Responses to the Novel Human Betacoronavirus Lineage C Virus in Human Ex Vivo Respiratory Organ Cultures*. **87**(12), 6604–6614. https://doi.org/10.1128/JVI.00009-13

Wang, Q., Qi, J., Yuan, Y., Xuan, Y., Han, P., Wan, Y., Ji, W., Li, Y., Wu, Y., Wang, J., Iwamoto, A., Woo, P. C. Y., Yuen, K. Y., Yan, J., Lu, G., and Gao, G. F. (2014). Bat origins of MERS-CoV supported by bat Coronavirus HKU4 usage of human receptor CD26. *Cell Host and Microbe*, **16**(3), 328–337. https://doi.org/10.1016/j.chom.2014.08.009

Wang, Y., Sun, J., Zhu, A., Zhao, J., and Zhao, J. (2018). *Current understanding of middle east respiratory syndrome coronavirus infection in human and animal models Current understanding of middle east respiratory syndrome coronavirus infection in human and animal models*. *July*. https://doi.org/10.21037/jtd.2018.03.80

Weiss, S. R., and Navas-Martin, S. (2005). Coronavirus Pathogenesis and the Emerging Pathogen Severe Acute Respiratory Syndrome Coronavirus. *Microbiology and Molecular Biology Reviews*, **69**(4), 635–664. https://doi.org/10.1128/mmbr.69.4.635-664.2005

WHO. (2013). *WHO guidelines for investigation of cases of human infection with Middle East Respiratory Syndrome Coronavirus*. *july*.

WHO. (2014). *Middle East respiratory syndrome coronavirus (MERS - CoV) summary and literature update – as of 9 May 2014*. **4***:* 1–8.

WHO. (2021). MERS Situation Update 2021. *Disease Outbreak News*, *May*, 22765492. http://www.emro.who.int/health-topics/mers-cov/mers-outbreaks.html

Widagdo, W., Okba, N. M. A., Stalin Raj, V., and Haagmans, B. L. (2017). MERS-coronavirus: From discovery to intervention. *One Health*, **3** :11–16. https://doi.org/10.1016/j.onehlt.2016.12.001

World Health Organization. (2017). *Middle East respiratory syndrome coronavirus (MERS-CoV) WHO MERS-CoV Global Summary and Assessment of Risk (Current Situation 21 July 2017)*. *June*, 8. http://www.who.int/emergencies/mers-cov/risk-assessment-july-2017.pdf?ua=1

Xia, Z., Zhang, J., Xue, Y., Sun, G., and Jin, Z. (2015). *Modeling the Transmission of Middle East Respirator Syndrome Corona Virus in the Republic of Korea*. 1–13. https://doi.org/10.1371/journal.pone.0144778

Yin, y., and Wunderink, A. R. G. (2018). Invited review series : respiratory infections in the asia-pacific region series editor : grant waterer mers, sars and other coronaviruses as causes of pneumonia. *Respiratory infections in the Asia-pacific region*, **23**(13196), 130–137. https://doi.org/10.1111/resp.13196

Ying, T., Du, L., Ju, T. W., Prabakaran, P., Lau, C. C. Y., Lu, L., Liu, Q., Wang, L., Feng, Y., Wang, Y., Zheng, B.-J., Yuen, K.-Y., Jiang, S., and Dimitrov, D. S. (2014). Exceptionally Potent Neutralization of Middle East Respiratory Syndrome Coronavirus by Human Monoclonal Antibodies. *Journal of Virology*, **88**(14), 7796–7805. https://doi.org/10.1128/jvi.00912-14

Yixuan J. Hou, et al. (2020). Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-. *Ann Oncol*, **1:**19–20.

Zaki, A. M., van Boheemen, S., Bestebroer, T. M., Osterhaus, A. D. M. E., and Fouchier, R. A. M. (2012). Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia. *New England Journal of Medicine*, **367**(19), 1814–1820. https://doi.org/10.1056/nejmoa1211721

Zhou, Z., Hui, K. P. Y., So, R. T. Y., Lv, H., Perera, R. A. P. M., Chu, D. K. W., Gelaye, E., Oyas, H., Njagi, O., Abayneh, T., Kuria, W., Walelign, E., Wanglia, R., Masry, I. El, Dobschuetz, S. Von, Kalpravidh, W., Chevalier, V., Miguel, E., Fassi-Fihri, O., Peiris, M. (2021). Phenotypic and genetic characterization of MERS coronaviruses from Africa to understand their zoonotic potential. *Proceedings of the National Academy of Sciences of the United States of America*, **118**(25). https://doi.org/10.1073/pnas.2103984118

Zohaib, A., Saqib, M., Athar, M. A., Chen, J., Sial, A. ur R., Khan, S., Taj, Z., Sadia, H., Tahir, U., Tayyab, M. H., Qureshi, M. A., Mansoor, M. K., Naeem, M. A., Hu, B. J., Khan, B. A., Ujjan, I. D., Li, B., Zhang, W., Luo, Y., Shi, Z. L. (2018). Countrywide Survey for MERS-Coronavirus Antibodies in Dromedaries and

Humans in Pakistan. *Virologica Sinica*, *33*(5), 410–417. https://doi.org/10.1007/s12250-018-0051-0

Zumla, A., Chan, J. F. W., Azhar, E. I., Hui, D. S. C., and Yuen, K. Y. (2016). Coronaviruses-drug discovery and therapeutic options. *Nature Reviews Drug Discovery*, **15**(5), 327–347. https://doi.org/10.1038/nrd.2015.37

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