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 website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
The COVID-19 pandemic – How many times were we warned before?

Naim Mahroum a,*, Isa Seida a, Sevval Nil Esirgin a, Nicola Luigi Bragazzi b

a International School of Medicine, Istanbul Medipol University, Göztepe Mah, Atatürk Cd. No:80, Beykoz, Istanbul 34810, Turkey
b Laboratory for Industrial and Applied Mathematics (LIAM), Department of Mathematics and Statistics, York University, Toronto, Canada

ARTICLE INFO

Keywords:
Coronaviruses
SARS
MERS
SARS-CoV-2
COVID-19

ABSTRACT

Infectious diseases are known to act in both predictable and unpredictable ways, which leads to the notions of emerging and reemerging infectious diseases. Emerging diseases with their disastrous consequences might be surprising and unpredictable, but they could be foreseen. For instance, some emerging diseases and recently the coronavirus disease 2019 (COVID-19) were the reason for papers published by the World Health Organization (WHO) and other researchers addressing the likely pathogens causing future outbreaks, according to the reports of the WHO in 2016 and 2018. Although it might seem like a wisdom in retrospect, several studies had already indicated possible future outbreaks caused by coronaviruses. Announcements, which may be viewed as “warnings,” appeared since the emergence of the first coronavirus-related outbreak caused by severe acute respiratory syndrome coronavirus (SARS-CoV) in the winter of 2002–2003 and a later outbreak caused by the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012–2013. Therefore, we were curious to review the medical literature prior to the COVID-19 pandemic with an aim to enumerate and evaluate studies addressing and warning against future outbreaks, and surprisingly pandemics, of members of coronaviruses. Interestingly, we found numerous studies that correctly predicted the current pandemic of COVID-19. While this part is highly interesting, how authorities reacted and prepared for warnings, if any, and how will they get prepared for the next warnings are our main messages. Taking these points into serious consideration will certainly aid in analyzing reports regarding possible future outbreaks as well as in developing various strategies for prevention and coping with such epidemics.

1. Introduction

As the pandemic of coronavirus disease 2019 (COVID-19) continues to emerge worldwide with no country being spared [1], scientists and researchers are relentlessly looking for the origin of SARS-CoV-2 [2]. However, previous outbreaks of coronaviruses, particularly the SARS epidemic that emerged in 2002 [3] and later the MERS outbreak in 2012 [4], might in fact be viewed as a warning of future human coronaviruses-related pandemics. The close resemblance of the viral genome structures of SARS-CoV-2 and SARS virus (SARS-CoV) [5] makes the assumption more accurate.

Coronaviruses with the subfamilies or genera designated as Alpha, Beta, Gamma, and Delta belong to the large family named “Coronaviridae” [6]. While not all the genera are human pathogens, human coronaviruses are mainly respiratory pathogens that cause a wide range of respiratory-related symptoms and diseases [7]. In addition, coronaviruses have shown through history, particularly in the last decades, their ability to mutate while passing through various species, eventually resulting in human pathogens responsible for several outbreaks such as SARS and MERS and even large pandemics as the COVID-19 pandemic [8]. A review of the medical literature long before the current pandemic of COVID-19 showed that a pandemic could emerge in the future caused by mutant members of the Coronaviridae, particularly those derived from bats [9]. Moreover, the characteristics of bat-derived coronaviruses and their ability to infect new species leading to human pathogens were previously reported [10].

In a timeline fashion and by dividing the time periods from the outbreak of SARS in 2002 to that of MERS in 2012 and then from MERS to the current COVID-19 pandemic, we reviewed the medical literature in terms of previous “warnings” or more precisely “predictions,” “announcements,” and reports of possible and probable future pandemics caused by members of the Coronaviridae family. The frequency of mention of those statements, the evidence presented, and the response of international organizations such as the World Health Organization (WHO) were analyzed and presented. The “pre-COVID-19” papers and studies concluding those aspects were viewed as warnings, and thus,
Roniviridae are families belonging to the Nidovirales order. The Coronaviridae family consists of 4 subgroups: Alpha, Beta, Gamma, and Delta coronaviruses (Fig. 1) [11]. All viruses in the Nidovirales order are non-segmented positive-sense RNA viruses having some of the largest genomes [12]. Members of the Nidovirales order are also known to have a highly conserved genomic organization with the following features: a large replicase gene preceding structural and ancestry genes, unique enzymatic activities encoded within a large replicase-transcriptase polyprotein, expression of many nonstructural genes by ribosomal frameshifting, and expression of downstream genes by synthesis of 3′ nested subgenomic mRNAs [13]. The differences in the members of the order lie in the numbers, types, and sizes of structural proteins. Such differences constitute the alterations in structure and morphology of the nucleocapsids and virions [7].

Initially, coronaviruses were believed to cause mild, self-limited respiratory infections in humans; however, the SARS outbreak proved that coronaviruses are capable of causing more severe respiratory symptoms [14]. Of the 4 established human coronaviruses, two originated from alphacoronaviruses, while the remaining two from betacoronaviruses. Interestingly, these viruses were isolated nearly 50 years ago [15–17]. It is important to note that Betacoronavirus is the genus from which SARS and MERS evolved.

1.2. Animal origin of human pathogenic coronaviruses

Retrospectively, epidemiological data showcased that the index case of SARS had contact history with game animals. Following that, serological studies revealed a higher prevalence of anti-SARS-CoV IgG antibodies in animal traders as compared to that in the general population [18]. Among animals in live markets, a racoon dog and masked palm civets (Paguma larvata) were initially highlighted for displaying SARS-CoV-like viruses almost identical to SARS-CoV [19]. Moreover, killing all masked civets in the markets resulted in a halt in reporting of SARS-CoV [20]. Wild or farm civets with no exposure to the animal markets were predominantly negative for SAR-CoV [21]. This indicated that masked civets are a potential augmenting intermediate host for SARS-CoV but are not likely to be the natural reservoir for the virus. Furthermore, 80% of the variety of species in the Guangzhou animal markets were shown to manifest anti-SARS-CoV antibodies [22]. The potential for these organisms to be an amplifying intermediate should not be ignored as all of these seem to be the final hosts for SARS-CoV [18].

Later, investigations identified similar coronavirus in bats, SARS-related Rhinolophus bat CoV HKU3 (SARSr-Rh-BatCoV HKU3), and Chinese horseshoe bats [23]. The horseshoe bats display anti-SARS-CoV antibodies alongside the genomic sequences of SARSr-Rh-BatCoV HKU3 [24,25]. The latter with other bat coronaviruses were shown to share 88–92% nucleotide sequence homology. In fact, these studies constitute the basis for the notion that bats could potentially be the host for emerging human pathogenic coronaviruses.

Similarly, phylogenetic cluster analysis showcased MERS-CoV belonging to the same group as bat CoV-HKU4 and CoV-HKU5. Like bat CoV-HKU4, MERS-CoV utilized the dipeptidyl peptidase 4 (DPP4) for the entry of virus into cells [26]. Studies highlighted RNA-dependent RNA polymerase sequences of MERS being phylogenetically similar to those in bat Beta-CoV obtained from Africa and Europe [27,28]. Studies in the Middle East and Africa illustrated dromedary camels to be seropositive for MERS-CoV-specific neutralizing antibodies [29,30]. Moreover, MERS-CoV isolated from nasal swabs of dromedary camels was positive for MERS-CoV-specific neutralizing antibodies [29,30]. More- over, MERS-CoV isolated from nasal swabs of dromedary camels was identical to the one found in humans. This further supported the theory addressing camels as the definitive reservoir of MERS [31]. In this regard, experimentally infected camels showed mild infection and massive viral shedding of MERS-CoV [32]. It is important to underline that camels shed MERS both through respiratory and fecal routes. Surprisingly, the majority of confirmed cases had no history of camel contact, which served to identify human-to-human transmission as the main source of infection or showcase the possibility of another route involving a currently unknown species [33].

Interestingly, SARS-CoV-2 shows more than 96% homology with bat CoV RaTG13 identified in Rhinolophus affinis bats [34]. However, the variations between SARS-CoV-2 and RaTG13 are significant to establish a parental relationship. This does not necessarily deny bats being the intermediate host for SARS-CoV-2, but it highlights that there could be another potential animal host, most likely among the species found in
the Wuhan seafood wholesale market, where many of the initial COVID-19 cases were located [35]. Recent studies presented a potential association with endangered small mammals known as Pangolins (Manis javanica) [36].

1.3. The 2002–2003 SARS outbreak

SARS was the first global outbreak of the 21st century with the first case reported in Foshan, China, in November 2002 [32]. The main symptoms of the disease were those mimicking influenza or atypical pneumonia, including fever, dry cough, malaise, myalgia, and headache [37]. Gastrointestinal symptoms and asymptomatic infections were also documented [38,39]. SARS-CoV caused mortality in some patients by progressing to pneumonia and respiratory failure [40]. The early cases were among people in the food industry and medical professions [41]. Infection occurred through either direct or indirect contact with patients. Until February 2003, the human-to-human transmission occurred only in mainland China. However, a physician, originally from Guangdong Province, who traveled to Hong Kong on February 21, 2003, while being infected with SARS-CoV transmitted the disease to 10 people in the hotel. Infected individuals spread the outbreak further to Hong Kong, Singapore, Canada, and Vietnam, leading to tertiary cases [42].

Following the spread, the WHO was notified by the end of February 2003. As a result, the WHO issued a global alert in March 2003 and established an international network of laboratories to reveal the etiological agent of the disease. A previously unrecognized coronavirus, SARS-CoV, was identified as the causative agent by April 2003 and subsequently sequenced by several laboratories [43]. The rapid sequencing of the virus with the help of cutting-edge molecular techniques and global efforts enabled to develop highly specific diagnostic tests and to track the pandemic [44]. By the beginning of the summer of 2003, SARS-CoV had spread to over 30 countries, causing 8096 reported cases and 774 deaths with a case fatality rate of approximately 10% [16]. China* and Hong Kong were the hot spots of the outbreak reporting most of the cases within the first 8 months of the outbreak. The WHO declared the pandemic is over in July 2003. Four additional cases were reported until late 2004, but none of them caused mortality or secondary spread [45].

In terms of origin, since the beginning of the outbreak, several studies have been conducted to reveal how SARS-CoV originated. Due to early epidemic studies indicating an animal origin, the efforts were focused on detecting SARS-CoV-like viruses among wildlife animals [45]. In 2003, Guan et al. [19] isolated SARS-CoV for the first time from Himalayan palm civets (HPCs) and a raccoon dog from a live animal market in Guangdong, China. At the same time, Li and colleagues [46] identified the metallopeptidase, angiotensin-converting enzyme 2 (ACE2) receptor as the functional receptor for SARS. The authors demonstrated that 5 proteins of SARS-CoVs isolated from infected civets and humans were capable of binding to human ACE2. Following these findings, the research community raised the question of whether civets are the natural reservoir or amplifying host. In 2005, two groups showed independently that horseshoe bats in the genus Rhinolophus are the natural reservoir of SARS-like coronaviruses [23,25]. Consequently, the medical community assumed that SARS-CoV originated from bats and was transmitted to humans via an intermediate host. To summarize, the features of SARS-CoV and the sequencing of its whole genome, the identification of the host receptor responsible for virus entry, the molecular characteristics of viral-host interaction, and studies for the development of diagnostic assays and vaccine candidates have been well documented.

1.4. Following the SARS outbreak

2003

On May 20, 2003, the WHO issued a report called “SARS: Status of the outbreak and lessons for the immediate future” [47]. In this report, the WHO warned that SARS could remain a threat for a variety of reasons such as:

1. SARS epidemiology is poorly understood, and diagnostic tests are limited, thereby making early detection difficult.
2. Difficulty of isolation and quarantine.
3. Coronaviruses are notorious for high mutation rates with an increased potential for outbreaks in the future.
4. Difficulties with vaccine development.

The WHO also identified the following concerns:

1. Inadequate surge capacity in hospitals and public health systems.
2. Healthcare providers themselves being the victims of the disease.
3. Shortage of expert staff to coordinate national and global responses to a rapidly evolving public health emergency.
4. In some cases, the need for hasty construction of new facilities; in other cases, hospitals being closed.
5. The power of poorly understood infectious diseases to incite widespread public anxiety and fear, social unease, economic losses, and unwarranted discrimination.
In June 2004, Snell [48] wrote that despite optimism regarding the novel respiratory viruses at that time, infections such as SARS and influenza still pose a risk. The study also highlighted the importance of areas of intensive livestock and marketing in propagating such infections. The author emphasized that because of the low infectivity of SARS, the epidemic could have been far more devastating if SARS showed more transmission rates.

SARS was addressed as an emerging infectious disease alongside other pathogens in a study on emerging viral diseases and infectious disease risks published in March 2006 [49].

Woo and colleagues [50] published an article titled “coronavirus diversity, phylogeny and interspecies jumping.” In their study, the authors showed that prior to the SARS outbreak, there were only 10 complete coronavirus genomes available. In contrast, by 2008, the number increased to 26 genomes. The genomes included human coronaviruses, bat coronaviruses, and coronaviruses native to other mammals. The study underlined rapid interspecies jumping of coronaviruses and the presence of more closely related coronaviruses among more distant organisms. The paper emphasized that interspecies jumping from zoonotic outbreaks could potentially reach humans and cause a devastating outbreak.

The 2012–2013 MERS outbreak

In June 2012, a novel coronavirus was isolated from the sputum of a 60-year-old man who had died from acute pneumonia in Jeddah, Saudi Arabia [37]. Due to its geographical appearance alongside severe respiratory symptoms, the isolated coronavirus was named as the Middle East respiratory syndrome coronavirus (MERS-CoV). MERS-CoV infection manifested as flu-like symptoms such as fever, myalgia, dry cough, malaise, and headache, similar to that of SARS-CoV. However, the infection could progress to pneumonia with acute respiratory distress syndrome, septic shock, and multiorgan failure with high mortality rates [51]. Asymptomatic infection was also documented [52]. According to the MERS situation update report issued by WHO in February 2022, a total of 2585 cases were reported globally and 890 of them died with a case-fatality rate of 34.4%, which is more than three times of the fatality rate of the SARS epidemic [53]. In contrast to SARS, the outbreak of MERS has not disappeared completely as new cases are still being reported in a continuous but slow manner, according to the report.

Even though the MERS epidemic reached more than 20 countries since its first discovery, the virus was endemic in Arabian Peninsula, and 80% of cases have occurred in Saudi Arabia [54]. In fact, the epidemiology of MERS infection showed a slow and continuous transmission in Arabian Peninsula with occasional flare in cases and limited outbreaks in different regions other than Arabian Peninsula. Because MERS-CoV infects humans through zoonotic transmission and human-to-human transmission is rare, the outbreaks are mostly limited to the Gulf region [55]. Nevertheless, secondary outbreaks of MERS were reported in other countries by travel, such as the outbreak in South Korea in 2015 [56]. These outbreaks, however, claimed to be caused by human-to-human transmission among household contacts and in healthcare settings [57]. In the case of the 2015 outbreak in South Korea, a single infected traveler spread the disease to healthcare professionals and other patients in the hospital, resulting in more than 180 hospital-related reported case [58].

The complete genome of MERS-CoV was sequenced and published in November 2012 [26]. In 2013, Raj et al. [59] identified the dipeptidyl peptidase 4 (DPP4; also known as CD26) as a functional receptor for MERS-CoV. Phylogenetic analysis of the novel virus revealed high similarity with the bat Betacoronaviruses: BtCoV-HKU4 and BtCoV-HKU5. Since the contact between bats and humans is not very likely in Arabian Peninsula, other intermediate hosts were considered. In this regard, the MERS-CoV has been isolated primarily from the nasal swabs of dromedaries in the Middle East, thus showing that camels are a potential source of MERS-CoV infection [60]. The researchers suggested that MERS-CoV originated in bats and were transmitted to camels in the past and then eventually transmitted to humans. However, MERS-CoV has never been isolated from bats; hence, the origin of the virus could not be fully revealed.

Following the MERS outbreak

Chan and colleagues [61] concluded that MERS-CoV, called HCoV-EMC at that time, is less transmissible than SARS-CoV, but urged healthcare authorities to remain alert and not to rule out a SARS-like
pandemic.

Based on the WHO recommendations at the time, Saudi Arabia issued no Hajj travel restrictions for the Hajj in October 2012 and issued recommendations only for proper hand hygiene and cough etiquette [62].

2013

In February 2013, the WHO issued a global alert and response update urging international communication regarding MERS infections and reporting all cases to the WHO [63].

In the same year, Ge et al. [64] isolated a live SARS-like coronavirus from bat which was capable of using ACE2 receptors for cell entry in humans, civets, and Chinese horseshoe bats. The authors provided the clearest evidence on the origin of SARS-CoV in bats by that time. Additionally, they highlighted the importance of developing pathogen discovery programs to detect high-risk wildlife groups and hotspots of disease emergence.

Furthermore, Graham and colleagues [65] in a paper titled “a decade after SARS,” summarized various strategies for coping and controlling emerging coronaviruses. The authors illustrated that several bat coronaviruses might be naturally able to enter human cells by recognizing the human orthologue receptors. The authors claimed that the growing density of human population made interaction with wild animal habitats easier. According to the study, an increase in the average age of the population and the number of immunocompromised patients facilitate the emergence of future coronavirus outbreaks. The importance of developing efficient strategies for rapid diagnosis and treatment and the development of vaccines against emerging coronavirus infections were addressed and emphasized.

2015

In 2015, Menachery and colleagues [66] demonstrated the potential pathogenicity of SARS-like coronavirus, SHC014-CoV, which circulated in Chinese horseshoe bat populations. The authors created a chimeric virus by merging SHC014-CoV spike protein with mouse-adapted SARS-CoV backbone. The chimeric viruses efficiently bound to human ACE2 receptor orthologs and replicated in primary human airway cells, eventually achieving in vitro titers equivalent to the epidemic strains of SARS-CoV. The study concluded that SARS-like coronaviruses that are capable of entry into human cells through ACE2 receptors pose a great risk for the emergence of new coronavirus outbreaks.

By the end of the same year, 2015, a group of WHO experts met in a workshop in Geneva to prepare an initial list of the top emerging pathogens likely to cause severe outbreaks in the near future. Among other viruses listed, highly pathogenic emerging coronaviruses relevant to humans such as SARS and MERS-CoV were mentioned [67]. The list was prepared under the platform of the research and development (R&D) Blueprint, which was established by WHO to increase preparedness for future epidemics. According to the R&D Blueprint, the WHO works to develop R&D roadmaps for each pathogen in the priority list. This list is updated regularly, where the last version mentioned COVID-19 as the first issue to deal with, alongside SARS and MERS-CoV [68].

2016

The WHO convened to declare a plan of action to support and elaborate on R&D Blueprint. During the meeting, infectious disease epidemics were addressed as a clear and persistent risk to global health and economy [69]. The members recognized the importance of research as an essential weapon in the fight against any epidemic. Most importantly, the methodology of preparing the priority pathogen list was determined in the meeting. The methodology employed Delphi technique, questionnaires, multi-criteria decision analysis, and expert review to identify relevant pathogens likely to cause future outbreaks.

2017

In January 2017, the WHO R&D Blueprint meeting was conducted to review the list of priority diseases. Virologists, bacteriologists, vaccinologists, public and animal health professionals, and infectious disease clinicians gathered to update the pathogen list based on the tailored prioritization methodology that was established in 2016. Unsurprisingly, SARS and MERS-CoV maintained their places in the updated version of the list [70].

In November 2017, Hu et al. [71] carried out a 5-year surveillance of SARS-related coronaviruses (SARSr-CoVs) in a cave inhabited by multiple species of horseshoe bats in Yunnan Province, China. Three new SARSr-CoVs capable of using human ACE2 receptors for cell entry were identified. The authors warned that recombination within the species inhabiting the cave may lead to future emergence of SARS-like outbreaks.

2018

In 2018, the WHO issued a report titled “MERS Global Summary and Assessment of Risk” [54]. In this report, the WHO warned against the emergence of new MERS outbreaks and provided preventive recommendations. The most urgent needs mentioned to prevent large MERS-CoV outbreaks were as follows:

1. To develop a better understanding of the transmission of MERS-CoV from animals and environmental sources to humans.
2. To identify risk factors for human or environmental infection in the workplace and health care settings.
3. To improve community studies and surveillance for community-acquired pneumonia.

In the same year, R&D Blueprint updated the priority list for pathogens based on the same methodology mentioned earlier [72]. Again, highly pathogenic emerging coronaviruses relevant to humans, including SARS-CoV and MERS-CoV, were present among the six other diseases in the list [73]. The prioritization criteria were mainly based on human transmissibility, medical countermeasures, disease severity, and human/animal interface.

1.7. The pre-COVID-19 period

The year 2019, the year COVID-19 emerged, was surprisingly the year important papers were published addressing a possible emergence of a large outbreak related to coronaviruses, months before the pandemic started. These are summarized as follows:

- In February 2019, Wang and Anderson [74] stated that bats are one of the richest virus reservoirs among mammals in terms of viral diversity, physiological variations in their body temperature, diverse habitats, and dietary preferences. The authors speculated that future outbreaks are more likely to develop from bat-borne viruses by assessing the spillover risk of the new strains of bat viruses related to ones that caused outbreaks in humans before. They concluded that among all bat viruses, coronaviruses pose the highest risk of emerging new outbreaks because of its great genetic diversity, large RNA genome carrying high mutation chance, and its previous spill-overs to humans and animals.
- In February 2019, Wong and colleagues [75] listed features of bats making them the number one suspect of zoonotic transmission of viruses to humans. In their article, the authors stated that bats have the second largest number of species among all mammals. According to the authors, the great genetic diversity of bats enables them to harbor a large variety of viruses enhancing the chance of interspecies virus transmission. Furthermore, the flying capability of bats enables them to transmit the viruses they harbor to long distances and to different species. The authors focused on the interspecies jumping of bat coronaviruses and pointed out the wildlife wet markets and restaurants in Southern China as a potential location for the next bat to human spillover events. Finally, the authors suggested more detailed and comprehensive surveillance of risky geographical areas to predict and prevent future coronavirus outbreaks in humans.
- Fan et al. [76] published a paper on viral diversity, reservoir hosts, and the geographical distributions of bat coronaviruses in China in
March 2019, 9 months before the first reported SARS-CoV-2 case. To the best of our knowledge, this is the last study or “warning” against a possible outbreak before the COVID-19 pandemic started. The authors reported that 10% of bats in China were positive for SARS-associated CoV nucleotide, and some of the viruses which they can carry can use ACE2 receptor for entry to the human cells as SARS-CoV. In their paper, the authors warned against a potential spillover of the SARS-CoV-resembling bat coronaviruses to humans where China could be the source of a new emerging outbreak.

A summary of the reports and papers addressing and warning against future outbreaks related to coronaviruses is presented in Table 1. Similarly, in a timeline presentation, the leading papers and reports are illustrated in Fig. 2.

2. Conclusion

Previous warnings against a future outbreak of members of the coronaviruses were numerous and generated by independent researchers as well as by the WHO and the R&D Blueprint forum. For instance, the importance and valuable efforts made by the R&D Blueprint under the WHO, their meetings, list of priority pathogens, and the messages concluded cannot be overemphasized. The WHO 2003 report regarding the SARS epidemic almost perfectly applies to the COVID-19 pandemic that emerged 17 years later, in terms of concerns and need of actions. Unfortunately, the calls of the WHO for increased medical infrastructure, hospital capacity, and adequate supply of PPE remained largely unanswered from the original SARS epidemic. The response for such calls and warnings were in fact very few to absent. This leaves no largely unanswered from the original SARS epidemic. The response for such calls and warnings were in fact very few to absent. This leaves no

Declaration of Competing Interest

The authors declare no competing interests.

References

[1] Organization WH. WHO Coronavirus (COVID-19) dashboard 2022 [Available from: https://covid19-who.int].
[2] Sallam VS, Wright JA, Vedel PY, Nair S, Li C, Kandimalla M, et al. COVID-19 transmission, current treatment, and future therapeutic strategies. Mol Pharm 2021;18(3):754–71.
[3] Cavalcuja S, Faubide M, Schirrmanhausen J. SARS: current overview, aetiology and epidemiology. Boin J Basic Med Sci 2003;3(2):46–55.
[4] Al-Tawfiq JA. Middle east respiratory syndrome-coronavirus infection: an overview. J Infect Public Health 2013;6(5):319–22.
[5] Rahman AA, Al-Ahmed SH, Haque S, Sah R, Tawari R, Malik YS, et al. SARS-CoV-2, SARS-CoV, and MERS-CoV: a comparative overview. Infec Med 2020;28(2):174–84.
[6] Cai J, Li F, Shi ZL. origin and evolution of pathogenic coronaviruses. Nat Rev Microbiol 2015;17(3):181–92.
[7] Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol 2015;1282:1–23.
[8] Shi Y, Wang G, Cai XP, Deng JW, Zheng J, Zhu HH, et al. An overview of COVID-19. J Zhejiang Univ Sci B 2020;21(3):343–60.
[9] Ye ZW, Yuan S, Yuan KS, Fung SY, Chan CP, Jin DY. Zoonotic origins of human coronaviruses. J Virol 2020;16(10):1688–97.
[10] Foroni D, Capulini R, Cerchia M, Gatti M. Molecular evolution of human coronavirus genomes. Trends Microbiol 2017;25(1):35–48.
[11] Brian DA, Baric RS. Coronavirus genome structure and replication. Curr Top Microbiol Immunol 2005;287:3–130.
[12] Hantetian F, Nandakumar D, Lai A, Li M, Tucker JM, Glavisinaiger BA. The molecular virology of coronaviruses. J Biol Chem 2020;295(9):12910–34.
[13] Snijder EJ, Decroly E, Zieheburg J. The nonstructural proteins directing coronavirus RNA synthesis and processing. Adv Virus Res 2016;96:126–68.
[14] Lam CW, Chan MH, Wong CK. Severe acute respiratory syndrome: clinical and laboratory manifestations. Clin Biochem Rev 2004;25(2):121–32.
[15] Hamre D, Procknow J. A new virus isolated from the human respiratory tract. Proc Soc Exp Biol Med 1966;121(1):190–3.
[16] Bradburne AF, Bynoe ML, Tyrrell DA. Effects of a “new” human respiratory virus in volunteers. Br Med J 1967;3(5568):767–9.
[17] McIntosh K, Becker WB, Chanock RM. Growth in suckling-mouse brain of “IBV-like” viruses from patients with upper respiratory tract disease. Proc Natl Acad Sci U S A 1967;66(5):76–9.
[18] Centers for Disease C, Prevention. Prevalence of IgG antibody to SARS-associated coronavirus in animal traders-Guangdong Province, China, 2003. MMWR Morb Mortal Wkrly Rep 2003;52(41):986–7.
[19] Guan Y, Zheng BJ, He QY, Liu XL, Zhuang ZX, Cheung CL, et al. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. Science 2003;305(5683):276–8.
[20] Kan B, Wang M, Jing H, Xu H, Jiang X, Yan M, et al. Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. J Virol 2005;79(18):11892–905.
[21] Poon LL, Chu DK, Chan KH, Wong OK, Ellis TM, Leung YH, et al. Identification of a novel coronavirus in bats. J Virol 2005;79(4):2001–9.
[22] Tu C, Cramer GI, Kong X, Chen J, Sun Y, Yu M, et al. Antibodies to SARS coronavirus in civets. Emerg Infect Dis 2004;10(12):2244–5.
[23] Lau SK, Woo PC, Li KS, Huang Y, Tsoi HW, Wong JH, et al. Severe acute respiratory syndrome-coronavirus-like virus in Chinese horseshoe bats. Proc Natl Acad Sci U S A 2005;102(39):14040–5.
[24] Lau SK, Woo PC, Yip CC, Tse H, Tsoi HW, Cheng VC, et al. Coronaviruses HKU1 and other coronavirus infections in Hong Kong. J Clin Microbiol 2006;44(6):2063–71.
[25] Li W, Shi Z, Yu M, Ren W, Smith C, Epstein JH, et al. Bats are natural reservoirs of SARS-like coronaviruses. Science 2005;310(5748):676–9.
[26] van Boheemen S, de Graaf M, Lauber C, Bestebroer TM, Raj VS, Zaki AM, et al. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. MBio 2012;3(6).
[27] Annan A, Baldwin HJ, Corman VM, Klose SM, Ouwens M, Nkrumah AM, et al. Human betacoronavirus 2c: clinical and epidemiological studies. Lancet Infect Dis 2013;13(10):859–66.
[28] Raj VS, Farag EA, Reusken CB, Lamers MM, Pas SD, Voermans J, et al. Isolation of Middle East respiratory syndrome coronavirus neutralising serum antibodies in dromedary camels: a comparative serological study. Lancet Infect Dis 2013;13(10):736–42.
[29] Chan JF, Lau SK, To KK, Cheng VC, Woo PC, Yuen KY. Middle East respiratory syndrome coronavirus: another zoonotic coronavirus causing SARS-like disease. Clin Microbiol Rev 2015;28(2):665–522.
[30] Reusken CB, Haagmans BM, Muller MA, Gudelje C, Godeke GJ, Meyer B, et al. Middle East respiratory syndrome coronavirus and metapneumovirus infection in dromedary camels: a comparative serological study. Lancet Infect Dis 2013;13(10):736–42.
[31] Adney LR, Lifko M, Ragan IK, Scott D, van Doremalen N, Boven RA, et al. Bovine coronaviruses shed large quantities of Middle East respiratory syndrome coronavirus (MERS-CoV) after experimental infection. Emerg Microbes Infect 2014;3(1):717–23.
[32] Samara EM, Abdoun KA. Concerns about misinterpretation of recent scientific data implicating dromedary camels in epidemiology of Middle East respiratory syndrome (MERS). MBio 2014;5(4). e01430-14.
[33] Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a novel coronavirus of probable bat origin. Nature 2020;579(7798):479–32.
[34] Wacharapluesadee S, Tan CW, Maneenon P, Duangkae P, Zhu F, Joyjinda Y, et al. Evidence for SARS-CoV-2 related coronaviruses circulating in bats and pangolins in Southeast Asia. Nat Commun 2021;12(1):972.
[35] Peiris JS, Chu CM, Cheng VC, Chan KS, Hung IF, Poon LL, et al. Clinical progression and viral load in a community outbreak of coronavirus-associated SARS pneumonia: a prospective study. Lancet 2003;361(9371):1767–72.
[36] Leung GM, Lim WW, Ho LM, Lam TH, Ghanji AC, Donnelly CA, et al. Seroprevalence of IgG antibodies to SARS-CoV in asymptomatic or subclinical population groups. Epidemiol Infect 2006;134(2):211–21.
