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Coronavirus (COVID-19): A Pandemic Disorder

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ABSTRACT

The Coronavirus disease 19 (COVID 19) is a highly transmitted and pathogenic viral infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is emerged in Wuhan, China and spread around the world. Genomic analysis revealed that SARS-CoV-2 is phylogenetically related to severe acute respiratory syndrome-like (SARS-like) bat viruses, therefore bats could be the possible primary reservoir. The intermediate source of origin and transfer human to human transfer has been confirmed widely. There is no clinically approved antiviral drug or vaccine available to be used against COVID-19. However, few broad-spectrum antiviral drugs have been evaluated against COVID-19 in clinical trials, resulted in clinical recovery. In the current review, we summarize and comparatively analyze the emergence and pathogenicity of COVID-19 infection and previous human coronavirus severe acute respiratory syndrome coronavirus (SAR-CoV) and middle east respiratory syndrome coronavirus (MERS-CoV). The rapid spread of the coronavirus disease 2019 (COVID-19), caused by a zoonotic beta-coronavirus entitled 2019 novel coronavirus (2019-nCoV), has become a global threat. This virus was reported to be a member of the b group of coronaviruses. The novel virus was named as Wuhan coronavirus or 2019 novel coronavirus (2019-nCov) by the Chinese researchers.

INTRODUCTION

Coronavirus derived from the Latin *corona* meaning "*Crown*" or "*halo*" which refers to characteristics appearance reminiscent of a crown or a solar corona around the virions (virus particles) when viewed under 2-D Transmission Electron Microscope(TEM), due to the surface covering in club-shaped protein spikes.

Coronaviruses belong to the ***Coronaviridae*** family in the ***Nidovirales*** order. Corona represents crown-like spikes on the outer surface of the virus; thus, it was named as a coronavirus.

Coronavirus (COVID-19)

Coronavirus disease 2019(COVID-19) is an emerging disease with a rapid increase in cases and deaths since its first identification in Wuhan, China, in December 2019. Limited data are available about coronavirus disease 2019 during pregnancy; however, information on illnesses associated with other highly pathogenic coronaviruses (ie, severe acute respiratory syndrome and the Middle East respiratory syndrome) might provide insights into coronavirus disease 2019's effects during pregnancy. Coronaviruses cause illness ranging in severity from the common cold to severe respiratory illness and death. Currently, the primary epidemiologic risk factors for coronavirus disease 2019 include travel from mainland China (especially Hubei Province) or close contact with infected individuals within 14 days of symptom onset. Data suggest an incubation period of w5 days (range, 2e14 days). Average age of hospitalized patients has been 49e56 years, with a third to half with an underlying illness. Children have been rarely reported. Men were more frequent among hospitalized cases (54e73%). Frequent manifestations include fever, cough, myalgia, headache, and diarrhea. Abnormal testing includes abnormalities on chest radiographic imaging, lymphopenia, leukopenia, and thrombocytopenia. Initial reports suggest that acute respiratory distress syndrome develops in 17e29% of hospitalized patients. Overall case fatality rate appears to bew1%; however, early data may overestimate this rate. In 2 reports describing 18 pregnancies with coronavirus disease 2019, all were infected in the third trimester, and clinical findings were similar to those in non-pregnant adults. Fetal distress and preterm delivery were seen in some cases. All but 2 pregnancies were cesarean deliveries and no evidence of in utero transmission was seen. Data on severe acute respiratory syndrome and Middle East respiratory syndrome in pregnancy are sparse. For severe acute respiratory

syndrome, the largest series of 12 pregnancies had a case-fatality rate of 25%. Complications included acute respiratory distress syndrome in 4, disseminated intravascular coagulopathy in 3, renal failure in 3, secondary bacterial pneumonia in 2, and sepsis in 2 patients. Mechanical ventilation was 3 times more likely among pregnant compared with nonpregnant women. Among 7 first-trimester infections, 4 ended in spontaneous abortion. Four of 5 women with severe acute respiratory syndrome after 24 weeks' gestation delivered preterm. For Middle East respiratory syndrome, there were 13 case reports in pregnant women, of which 2 were asymptomatic, identified as part of a contact investigation; 3 patients (23%) died. Two pregnancies ended in fetal demise and 2 were born preterm. No evidence of in utero transmission was seen in severe acute respiratory syndrome or Middle East respiratory syndrome. Currently, no coronavirus-specific treatments have been approved by the US Food and Drug Administration. Because coronavirus disease 2019 might increase the risk for pregnancy complications, management should optimally be in a health care facility with close maternal and fetal monitoring. Principles of management of coronavirus disease 2019 in pregnancy include early isolation, aggressive infection control procedures, oxygen therapy, avoidance of fluid overload, consideration of empiric antibiotics (secondary to bacterial infection risk), laboratory testing for the virus and coinfection, fetal and uterine contraction monitoring, early mechanical ventilation for progressive respiratory failure, individualized delivery planning, and a team-based approach with multispecialty consultations.

History of Coronavirus[2]

In 2003, China reported SARS-CoV, was infected with a virus causing Severe Acute Respiratory Syndrome (SARS) in Guangdong province. The virus was confirmed as a member of the Betacoronavirus subgroup and was named SARS-CoV. The infected patients exhibited pneumonia symptoms with a diffused alveolar injury which lead to Acute Respiratory Distress Syndrome (ARDS). SARS initially emerged in Guangdong, China and then spread rapidly around the globe with more than 8000 infected persons and 776 deceases.

A decade later in 2012, a couple of Saudi Arabian nationals were diagnosed to be infected with another coronavirus. The detected virus was confirmed as a member of coronaviruses and named as the Middle East Respiratory Syndrome Coronavirus.

(MERS-CoV). The World health organization reported that MERScoronavirus infected more than 2428 individuals and 838 deaths. MERS-CoV is a member beta-coronavirus subgroup

and phylogenetically diverse from other human-CoV. The infection of MERS-CoV initiates from a mild upper respiratory injury while progression leads to severe respiratory disease. Similar to SARScoronavirus, patients infected with MERS-coronavirus suffer pneumonia, followed by ARDS and renal failure.

Recently, by the end of 2019, WHO was informed by the Chinese government about several cases of pneumonia with unfamiliar etiology. The outbreak was initiated from the Hunan seafood market in Wuhan city of China and rapidly infected more than 50 peoples. The live animals are frequently sold at the Hunan seafood market such as bats, frogs, snakes, birds, marmots and rabbits. On 12th January 2020, the National Health Commission of China released further details about the epidemic, suggested viral pneumonia. From the sequence-based analysis of isolates from the patients, the virus was identified as a novel coronavirus. Moreover, the genetic sequence was also provided for the diagnosis of viral infection. Initially, it was suggested that the patients infected with Wuhan coronavirus induced pneumonia in China may have visited the seafood market where live animals were sold or may have used infected animals or birds as a source of food. However, further investigations revealed that some individuals contracted the infection even with no record of visiting the seafood market. These observations indicated a human to the human spreading capability of this virus, which was subsequently reported in more than 100 countries in the world. The human to the human spreading of the virus occurs due to close contact with an infected person, exposed to coughing, sneezing, respiratory droplets or aerosols.

These aerosols can penetrate the human body (lungs) *via* inhalation through the nose or mouth.

Virology and origin[1]

Coronavirus belongs to the subfamily Orthocoronavirinae in the family of Coronaviridae in the order Nidovirales, which mainly caused infections in respiratory and gastrointestinal tract. The 2019-nCoV is a novel enveloped beta-coronavirus which has a single stranded positive sense RNA genome(Zhu *et al*., 2020). Concerning the origin of the virus, several phylogenetic analysis suggested the bat to be the most probable animal reservoir. Based on genome sequencing, 2019-nCoV is about 89% identical to bat SARS-like-CoVZXC21, 82% identical to human SARS-CoV and about 50% to MERS-CoV(Chan et al., 2020; Lu et al., 2020). As both SARS-CoV and MERS-CoV were transmitted from bats to palm civets or

dromedary camels, and finally to humans, there should be another animal representing as an intermediate host between bat and human. Pangolins were suggested as the possible intermediate hosts, because their genome had approximately 85.5%-92.4% similarity to 2019-nCoV, representing two sub-lineages of 2019-nCoV in the phylogenetic tree, one of which (GD/P1L and GDP2S) was extremely closely related to 2019-nCoV(Lam *et al.*, 2020). Other research suggested 2019-nCoV was the recombinant virus of bat coronavirus and snake coronavirus, by comparison in conjunction with relative synonymous codon usage bias among different animal species(Ji *et al.*, 2020). The truth is yet to be discovered. The spike surface glycoprotein of coronavirus plays an essential role in binding to receptors on host cells and determines host tropism. Spike protein(S-protein) of 2019-nCoV is reported to bind with angiotensin-converting enzyme 2 (ACE2), the same receptor of SARS-CoV to invade host cells; whereas MERS-CoV uses dipeptidyl peptidase 4 (DPP4) as the primary receptor(Wu et al., 2020). The amino acid sequence of S-protein in 2019-nCoV is 76.47% identical to that of SARS-CoV, with the same structural confirmation and electrostatic properties in the interaction interface. The residues at positions 442, 472, 479, 487, and 491 in S-protein are reported to be at receptor complex interface with ACE2. However, four of the five critical residues in the 2019-nCoV S-protein are not preserved except for Tyr491. The binding free energy for 2019-nCoV S-protein to bind with human ACE2, increases by 28 kcal mol–1 compared to SARS-CoV S-protein (-50.6kcal mol–1 vs. -78.6kcal mol–1), due to the loss of hydrogen bond interactions by replacing Arg426 with Asn426(Xu *et al.*, 2020a). Furin-like cleavage site was supposed to be cleaved by proprotein convertase furin at special viral envelope glycoproteins, thereby enhancing viral fusion with host cell membranes. Coutard and colleagues (2020) reported a furin-like cleavage site in the S-protein of 2019-nCoV, which is absent in other lineage b beta-coronaviruses.

Another research team also discovered an “RRAR” furin recognition site by an insertion in the S1/S2 protease cleavage site in 2019-nCoV, instead of a single arginine in SARS-CoV. After quantifying the kinetics mediating the interaction via surface plasmon resonance, ACE2 is calculated to bind to 2019-nCoV ectodomain with ~15 nM affinity, which is approximately 10- to 20-fold higher affinity than ACE2 binding to SARS-CoV(Wrapp *et al.*, 2020). In all, the binding affinity between 2019-nCoV S-protein and ACE2 is comparable or even stronger than SARS-CoV S-protein and ACE2. This may explain the rapid development and strong ability of human-to-human transmission in COVID-19.

Taxonomy

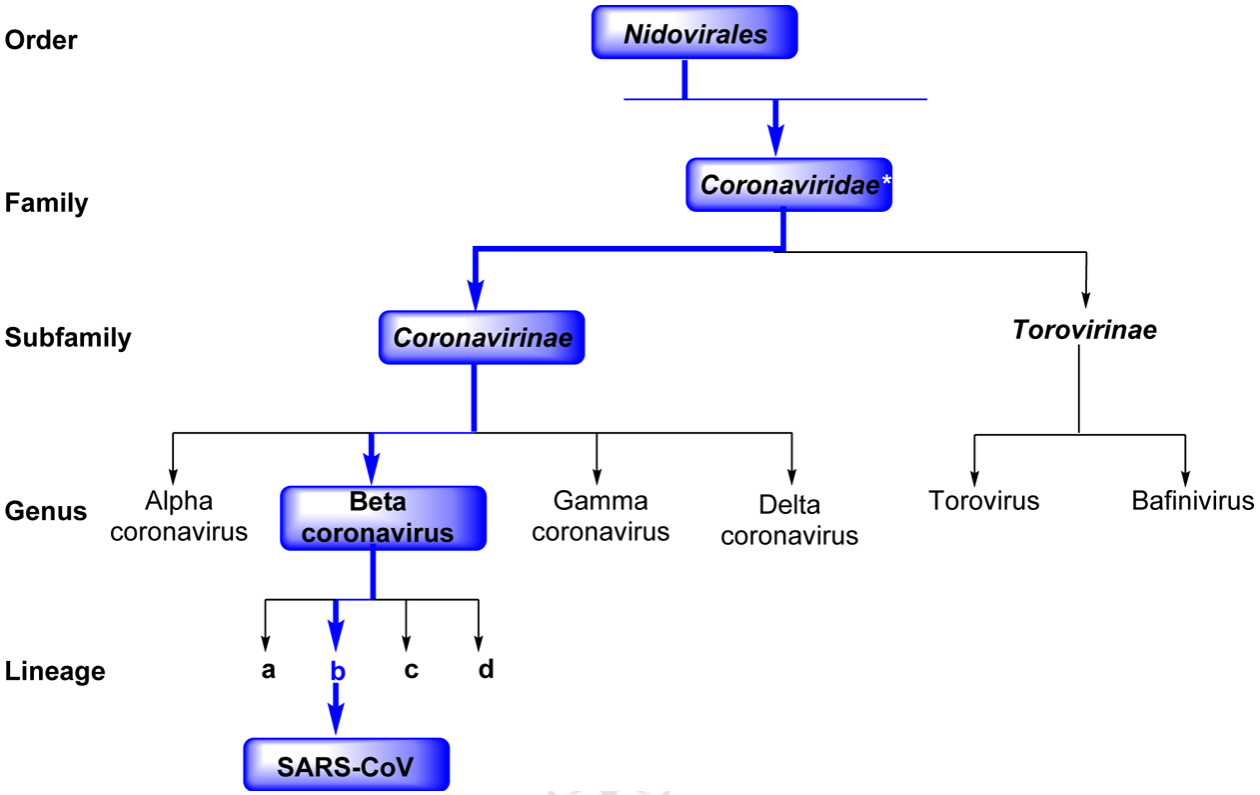

Figure No. 1: Schematic representation of the taxonomy of Coronaviridae (according to the International Committee on Taxonomy of Viruses). SARS-CoV belongs to the Betacoronavirus family but has a "b" lineage. *Coronaviridae, along with Arteriviridae, Mesoniviridae, and Roniviridae, are members of this family.

Structure of Coronavirus[3]

Coronaviruses are minute in size (65–125 nm in diameter) and contain a single-stranded RNA as a nucleic material, size ranging from 26 to 32kbs in length. The subgroups of coronaviruses family are alpha (a), beta (b), gamma (c) and delta (d) coronavirus. The severe acute respiratory syndrome coronavirus (SARS-CoV) H5N1 influenza A, H1N1 2009 and Middle East respiratory syndrome coronavirus (MERS-CoV) cause acute lung injury (ALI) and ARDS which leads to pulmonary failure and result in fatality. These viruses were thought to infect only animals until the world witnessed a SARS outbreak caused by SARS-CoV, 2002 in Guangdong, China.

The betacoronavirus genome encodes several structural proteins, including the glycosylated spike (S) protein that functions as a major inducer of host immune responses. This S protein

mediates host cell invasion by both SARS-CoV and SARS-CoV-2 via binding to a receptor protein called ACE2 located on the surface membrane of host cells. A recent study also revealed that this invasion process requires S protein priming which is facilitated by the host cell produced serine protease TMPRSS211. In addition, the viral genome also encodes several nonstructural proteins including RNA-dependent RNA polymerase (RdRp), coronavirus main protease (3CLpro), and papain-like protease (PLpro). Upon entrance to the host cells, the viral genome is released as a single-stranded positive RNA. Subsequently, it is translated into viral polyproteins using host cell protein translation machinery, which are then cleaved into effector proteins by viral proteinases 3CLpro and PLpro.1 PLpro also behaves as a deubiquitinase that may deubiquinate certain host cell proteins, including interferon factor 3 and NF-κB, resulting in immune suppression. RdRp synthesizes a full-length negative-strand RNA template to be used by RdRp to make more viral genomic RNA. The interaction between viral S protein and ACE2 on the host cell surface is of significant interest since it initiates the infection process. Cryo-EM structure analysis has revealed that the binding affinity of SARS-CoV-2 S protein to ACE2 is about 10−20 times higher than that of SARS-CoV S protein.[10] It is speculated that this may contribute to the reported higher transmissibility and contagiousness of SARS-CoV-2 as compared to SARS-CoV. The prospect also exists for discovery of therapeutic agents targeting the highly conserved proteins associated with both SARS-CoV and SARS-CoV-2.RdRp and 3CLpro protease of SARS-CoV-2 share over 95% of sequence similarity with those of SARS-CoV despite the fact that these two viruses demonstrate only 79% sequence similarity at the genome level.16 On the basis of sequence alignment and homology modeling, SARS-CoV and SARS-CoV-2 share a highly conserved receptor-binding domain (RBD), a domain of S protein, and 76% of sequence similarity in their S proteins. In addition, although the PLpro sequences of SARS-CoV-2 and SARS-CoV are only 83% similar, they share similar active sites. To date, there are no SARS-CoV-2-specific antiviral agents.

Researchers have been racing to find possible treatments to save lives and produce vaccines for future prevention. To support research and development efforts to discover effective therapeutic and preventive agents for COVID-19, CAS, a division of the American Chemical Society specializing in scientific information solutions, has analyzed scientific data related to the development of therapeutic agents and vaccines for human coronaviruses since 2003. The analyses presented in this report are based on the CAS content collection, a scientist-curated data collection covering published scientific literature and patents from over 60 patent

authorities worldwide. For a subset of the analyses, both CAS and MEDLINE data were collectively analyzed.

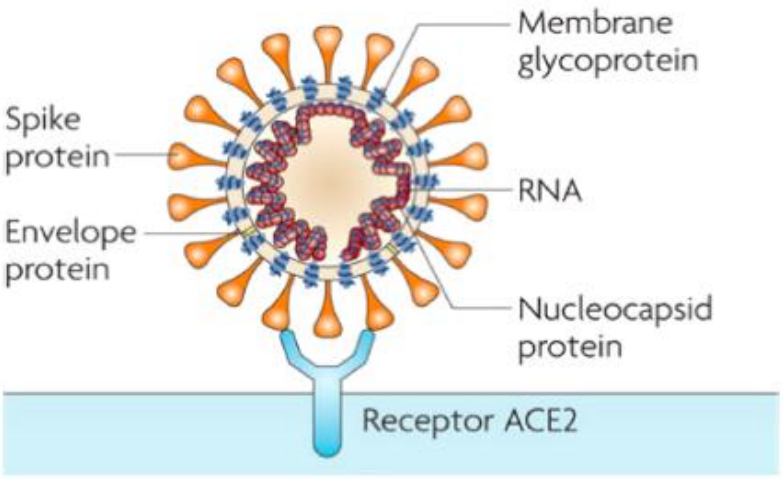

Figure No. 2: Cartoon illustration of the coronavirus structure and viral receptor ACE2 on the host cell surface. (Image was reproduced with permission from ref 9, Nature Reviews Microbiology 7(3), 226−236. Copyright 2009 Springer Nature.)

Generally speaking, viruses are essentially metastable, core-shell nanoparticles that are biologically produced in cells with a quite remarkable self-assembly process. The core is made of a coiled genomic polymer and tightly packaged in a protective protein shell called a capsid, which is tiled up by presynthesized subunits. For coronaviruses (Figure 2), such as those that cause SARS, MERS, and COVID-19, the RNA is directly complexed with and protected by a helical protein shell to form a coiled nucleocapsid. It is then enveloped by a lipid bilayer membrane decorated with various other proteins, such as the protruding "corona" spikes, which interact with the host cell. The biological function of viruses to preserve and, eventually, to deliver their nucleic acids to host cells depends on the virus's structural integrity. For example, for enveloped viruses, their lipid bilayer must stay intact throughout the pathways to keep them infectious. The protein capsid must be sufficiently strong to confine the elastically strained genomic coil and sufficiently tough to sustain osmotic pressure fluctuation in changing surroundings, yet they must be able to disassemble readily inside the host cells to release the genomic core. These constraints demand rather intricate protein building blocks that also must maintain desirable configurations to avoid malfunction. The envelope and capsid, however, can be compromised by an array of physical treatments, such as UV irradiation, heating, and desiccation, as well as by chemical

sanitization using acids, oxidants, alcohol, or some specialized surfactants. Approaches like these may seem relatively primitive; however, they can be extremely effective in slowing down or even preventing virus spread and transmission.

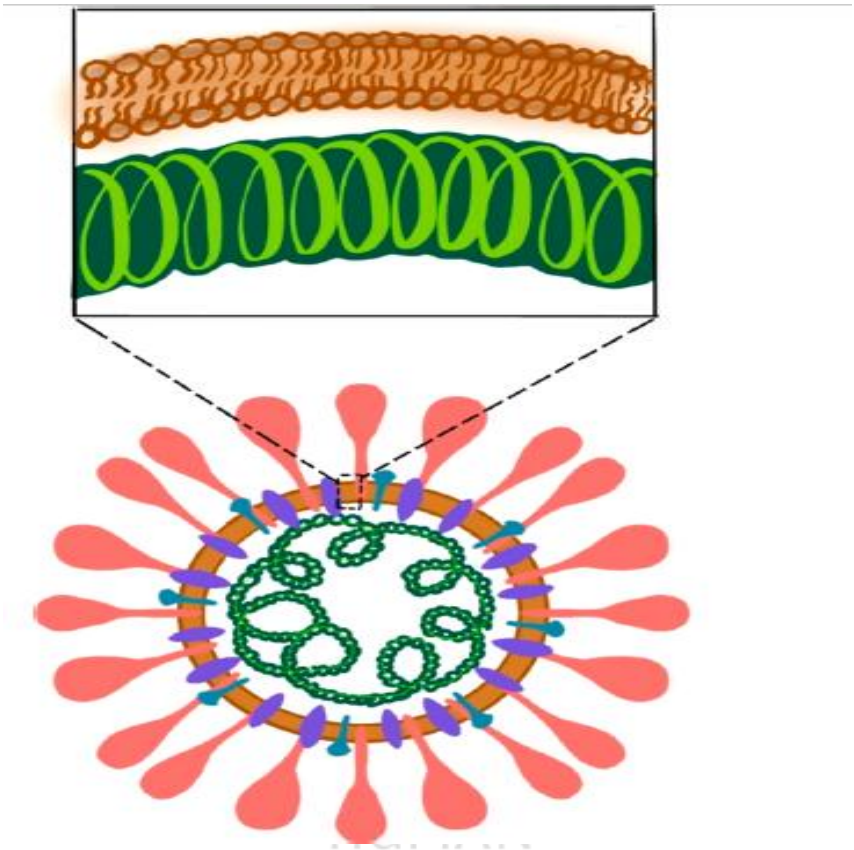

Figure No. 3: Structural model of a coronavirus particle, showing the nucleocapsid coil (green) inside an envelope (brown) with protruding spike proteins (red). The inset shows the bilayer structure of the envelope and a segment of the nucleocapsid.

Pathogenesis[4]

Pathogenesis

Animal Coronaviruses

Coronaviruses cause a large variety of diseases in animals, and their ability to cause severe disease in livestock and companion animals such as pigs, cows, chickens, dogs and cats led to significant research on these viruses in the last half of the 20th century. For instance, Transmissible Gastroenteritis Virus (TGEV) and Porcine Epidemic Diarrhea Virus (PEDV) cause severe gastroenteritis in young piglets, leading to significant morbidity, mortality, and ultimately economic losses. PEDV recently emerged in North America for the first time,

causing significant losses of young piglets. Porcine hemagglutinating encephalomyelitis virus (PHEV) mostly leads to enteric infection but has the ability to infect the nervous system, causing encephalitis, vomiting and wasting in pigs. Feline enteric coronavirus (FCoV) causes a mild or asymptomatic infection in domestic cats, but during persistent infection, mutation transforms the virus into a highly virulent strain of FCoV (Feline Infectious Peritonitis Virus, FIPV), that leads to development of a lethal disease called feline infectious peritonitis (FIP). FIP has wet and dry forms, with similarities to the human disease, sarcoidosis. FIPV is macrophage tropic and it is believed that it causes aberrant cytokine and/or chemokine expression and lymphocyte depletion, resulting in lethal disease [63]. However additional research is needed to confirm this hypothesis. Bovine CoV, Rat CoV, and Infectious Bronchitis Virus (IBV) cause mild to severe respiratory tract infections in cattle, rats, and chickens, respectively. Bovine CoV causes significant losses in the cattle industry and also has spread to infect a variety of ruminants, including elk, deer and camels. In addition to severe respiratory disease, the virus causes diarrhoea ('winter dysentery' and 'shipping fever'), all leading to weight loss, dehydration, decreased milk production, and depression. Some strains of IBV, a γ-coronavirus, also affect the urogenital tract of chickens causing renal disease. IBV significantly diminishes egg production and weight gain, causing substantial losses in the chicken industry each year. More recently, a novel coronavirus named SW1 was identified in a deceased Beluga whale. Large numbers of virus particles were identified in the liver of the deceased whale with respiratory disease and acute liver failure. Although, electron microscopic images were not sufficient to identify the virus as a coronavirus, sequencing of the liver tissue clearly identified the virus as a coronavirus. It was subsequently determined to be a γ-coronavirus based on phylogenetic analysis but it has not yet been verified experimentally that this virus. These viruses are highly divergent from other nidoviruses but are most closely related to the roniviruses. In size, they are ~20 kb, falling in between large and small nidoviruses. Interestingly, these viruses do not encode for an endoribonuclease, which is present in all other nidoviruses. These attributes suggest these viruses are the prototype of a new nidovirus family and maybe a missing link in the transition from small to large nidoviruses. Actually a causative agent of disease in whales. In addition, there has been intense interest in identifying novel bat CoVs, since these are the likely ultimate source for SARS-CoV and MERS-CoV, and hundreds of novel bat coronaviruses have been identified over the past decade [65]. Finally, another novel group of nidoviruses, *Mesoniviridae*, were recently identified as the first nidoviruses to exclusively infect insect hosts.

Human Coronaviruses

Prior to the SARS-CoV outbreak, coronaviruses were only thought to cause mild, self-limiting respiratory infections in humans. Two of these human coronaviruses are α-coronaviruses (HCoV-229E and HCoV-NL63) while the other two are β-coronaviruses (HCoV-OC43 and HCoV-HKU1). HCoV-229E and HCoV-OC43 were isolated nearly 50 years ago while HCoV-NL63 and HCoV-HKU1 were only recently identified following the SARS-CoV outbreak. These viruses are endemic in the human populations, causing 15–30% of respiratory tract infections each year. They cause more severe disease in neonates, the elderly, and in individuals with underlying illnesses, with a greater incidence of lower respiratory tract infection in these populations. HCoV-NL63 is also associated with acute laryngotracheitis (croup). One interesting aspect of these viruses is their differences in tolerance to genetic variability. HCoV-229E isolates from around the world have only minimal sequence divergence while HCoV-OC43 isolates from the same location but isolated in different years show significant genetic variability. This likely explains the inability of HCoV-229E to cross the species barrier to infect mice while HCoV-OC43 and the closely related bovine coronavirus, BCoV, are capable of infecting mice and several ruminant species. Based on the ability of MHV to cause demyelinating disease, it has been suggested that human CoVs may be involved in the development of multiple sclerosis (MS). However, no evidence to date suggests that human CoVs play a significant role in MS.

SARS-CoV, a group 2b β-coronavirus, was identified as the causative agent of the SARS outbreak that occurred in 2002–2003 in the Guangdong Province of China. It is the most severe disease caused by any coronavirus. During the 2002–2003 outbreak approximately 8098 cases occurred with 774 deaths, resulting in a mortality rate of 9%. This rate was much higher in elderly individuals, with mortality rates approaching 50% in individuals over 60 years of age. Furthermore, the outbreak resulted in the loss of nearly $40 billion dollars in economic activity, as the virus nearly shut down many activities in Southeast Asia and Toronto, Canada for several months. The outbreak began in a hotel in Hong Kong and ultimately spread to more than two dozen countries. During the epidemic, closely related viruses were isolated from several exotic animals including Himalayan palm civets and raccoon dogs. However, it is widely accepted that SARS-CoV originated in bats as a large number of Chinese horseshoe bats contain sequences of SARS-related CoVs and contain serologic evidence for a prior infection with a related CoV. In fact, two novel bat SARS-

related CoVs were recently identified that are more similar to SARS-CoV than any other virus identified to date. They were also found to use the same receptor as the human virus, ACE2, providing further evidence that SARS-CoV originated in bats. Although some human individuals within wet animal markets, had serologic evidence of SARS-CoV infection prior to the outbreak, these individuals had no apparent symptoms. Thus, it is likely that a closely related virus circulated in the wet animal markets for several years before a series of factors facilitated its spread into the larger population.

Transmission of SARS-CoV was relatively inefficient, as it only spread through direct contact with infected individuals after the onset of illness. Thus, the outbreak was largely contained within households and healthcare settings, except in a few cases of superspreading events where one individual was able to infect multiple contacts due to an enhanced development of high viral burdens or ability to aerosolize virus. As a result of the relatively inefficient transmission of SARS-CoV, the outbreak was controllable through the use of quarantining. Only a small number of SARS cases occurred after the outbreak was controlled in June 2003.

SARS-CoV primarily infects epithelial cells within the lung. The virus is capable of entering macrophages and dendritic cells but only leads to an abortive infection. Despite this, infection of these cell types may be important in inducing pro-inflammatory cytokines that may contribute to disease. In fact, many cytokines and chemokines are produced by these cell types and are elevated in the serum of SARS-CoV infected patients. The exact mechanism of lung injury and cause of severe disease in humans remains undetermined. Viral titers seem to diminish when severe disease develops in both humans and in several animal models of the disease. Furthermore, animals infected with rodent-adapted SARS-CoV strains show similar clinical features to the human disease, including an age-dependent increase in disease severity. These animals also show increased levels proinflammatory cytokines and reduced T-cell responses, suggesting a possible immunopathological mechanism of disease.

MERS-CoV is a group 2c β-coronavirus highly related to two previously identified bat coronaviruses, HKU4 and HKU5. It is believed that the virus originated from bats, but likely had an intermediate host as humans rarely come in contact with bat secreta. Serological studies have identified MERS-CoV antibodies in dromedary camels in the Middle East [96], and cell lines from camels have been found to be permissive for MERS-CoV replication providing evidence that dromedary camels may be the natural host. More convincing

evidence for this comes from recent studies identifying nearly identical MERS-CoVs in both camels and human cases in nearby proximities in Saudi Arabia. In one of these studies the human case had direct contact with an infected camel and the virus isolated from this patient was identical to the virus isolated from the camel [99]. At the present time it remains to be determined how many MERS-CoV cases can be attributed to an intermediate host as opposed to human-to-human transmission. It has also been postulated that human-to-camel spread contributed to the outbreak.

Outbreaks of Coronavirus Related Diseases

Outbreaks	Virus Type	Death
2003 SARS Outbreak	SARS-CoV	724
2012 MERS	MERS-CoV	Over 400
2015 MERS in South Korea	MERS-CoV	36
2018 MERS	MERS-CoV	41
2019-2020 Coroavirus Pandemic	SARS-CoV-2	At least 1,54,371

SCREENING AND PREVENTION

SCREENING

• At-risk populations

Screening of travelers from affected areas is being done under the guidance of public health authorities at airports to assure that persons who are ill are referred for medical evaluation and to educate those who are not ill but at risk for infection about self-monitoring.

Triage screening is recommended at points of medical care to identify patients with symptoms and exposure history that suggest the possibility of COVID-19, so that prompt isolation measures can be instituted.

• Screening tests

Screening and triage to isolation and testing with polymerase chain reaction are based on clinical presentation and exposure history:

– Presence of respiratory symptoms (cough, dyspnea) and fever (CDC, WHO).

– Recent (within 14 days) travel to or residence in any geographic areas with widespread COVID-19 (WHO, CDC).

– Close contact with a person with known or suspected COVID-19 while that person was ill (WHO, CDC).

Work in a health care setting in which patients with severe respiratory illnesses are managed, without regard to place of residence or history of travel (WHO).

–Unusual or unexpected deterioration of an acute illness despite appropriate treatment, without regard to place of residence or history of travel, even if another cause has been identified that fully explains the clinical presentation (WHO).

PREVENTION

There is no vaccine against COVID-19. Prevention depends on standard infection control measures, including isolation of infected patients. Quarantine may be imposed on asymptomatic exposed persons deemed by public health authorities to be at high risk

For the general public, avoidance of ill persons and diligent hand and cough hygiene are recommended. Physical distancing should be used as much as possible. Advise public as follows:

○ **If sick, stay home and call doctor**

Avoid large gatherings and unnecessary gatherings; stay home except for critical needs (eg, to resupply food and medicines) during acceleration phase of pandemic or subsequent regional flare-ups.

– Telecommute if nature of job makes it possible

When going out in public is unavoidable, cover mouth and nose with a cloth face cover (not with a mask meant for health care workers).

Greet others without touching; nod or wave instead of shaking hands or hugging. Try to maintain physical distance: at least 1 m (3 ft), preferably 2 m (6 ft).

Psychological and emotional toll of physical distancing from family and friends can be mitigated with nonphysical interaction (eg, phone calls, texting, video chats).

Wash hands often and thoroughly. Soap and water are best. High-alcohol hand sanitizers are acceptable until next possible hand washing.

○ Cover coughs. Use tissue and throw it away; second choice is sleeve, not hand.

○ Avoid touching face.

• Patients managed at home

Patient is encouraged to stay at home except to seek medical care, to self-isolate to a single area of the house (preferably with a separate bathroom), to practice good hand and cough hygiene, and to wear a face mask during any contact with household members.

Patients should be advised that if a need for medical care develops, they should call their health care provider in advance so that proper isolation measures can be undertaken promptly on their arrival at the health care setting.

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