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COVID -19 DISEASE SYMPTOMS AND CONTROL MEASURES

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ABSTRACT
Human coronaviruses, first characterized in the 1960s, are responsible for a substantial proportion of upper respiratory tract infections in children. Since 2003, at least 5 new human coronaviruses have been identified, including the severe acute respiratory syndrome coronavirus, which caused significant morbidity and mortality. NL63, representing a group of newly identified group I coronaviruses that includes NL and the New Haven coronavirus, has been identified worldwide. These viruses are associated with both upper and lower respiratory tract disease and are likely common human pathogens. The global distribution of a newly identified group II coronavirus, HKU1, has not yet been established. Coronavirology has advanced significantly in the past few years. The SARS epidemic put the animal coronaviruses in the spotlight. The background and history relative to this important and expanding research area are reviewed here.

KEYWORDS: Coronavirus, Covid-19, Pandemic disease, WHO guideline.

General Concept

The word was introduced by a group of virologists as a short article "Coronaviruses" in the "News and Views" section of *Nature* (vol. 220, no. 5168, November 16, 1968, p. 650): "…avian infectious bronchitis virus has a characteristic electron microscopic appearance resembling, but distinct from, that of myxoviruses. Particles are more or less rounded in profile…there is also a characteristic 'fringe' of projections 200 Å long, which are rounded or petal shaped, rather than sharp or pointed, as in the myxoviruses. This appearance, recalling the solar corona, is shared by mouse hepatitis virus….In the opinion of the eight virologists these viruses are members of a previously unrecognized group which they suggest should be called the coronaviruses, to recall the characteristic appearance by which these viruses are identified in the electron microscope."

Introduction and history

Coronaviruses are a group of related viruses that cause diseases in mammals and birds. In humans, coronaviruses cause respiratory tract infections that can be mild, such as some cases of the common cold (among other possible causes, predominantly rhinoviruses), and others that can be lethal, such as SARS, MERS, and COVID-19. Symptoms in other species vary: in chickens, they cause an upper respiratory tract disease, while in cows and pigs they cause diarrhea. There are yet to be vaccines or antiviral drugs to prevent or treat human coronavirus infections.

Coronaviruses constitute the subfamily *Orthocoronavirinae*, in the family *Coronaviridae*, order *Nidovirales*, and realm *Riboviria*. They are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The genome size of coronaviruses ranges from approximately 27 to 34 kilobases, the largest among known RNA viruses. The name *coronavirus* is derived from the Latin *corona*, meaning "crown" or "halo", which refers to the characteristic appearance reminiscent of a crown or a solar corona around the virions (virus particles) when viewed under two-dimensional transmission electron microscopy, due to the surface covering in club-shaped protein spikes.

Discovery

Human coronaviruses were first discovered in the late 1960s. The earliest ones discovered were an infectious bronchitis virus in chickens and two in human patients with the common cold (later named human coronavirus 229E and human coronavirus OC43). Other members of this family have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2004, HKU1 in 2005, MERS-CoV in 2012, and SARS-CoV-2 (formerly known as 2019- nCoV) in 2019. Most of these have involved serious respiratory tract infections.

Etymology

The name "coronavirus" is derived from Latin *corona*, meaning "crown" or "wreath", itself a borrowing from Greek κορώνη *korṓnē*, "garland, wreath". The name refers to the characteristic appearance of virions (the infective form of the virus) by electron microscopy, which have a fringe of large, bulbous surface projections creating an image reminiscent of a crown or of a solar corona. This morphology is created by the viral spike peplomers, which are proteins on the surface of the virus.

Classification

Coronaviruses vary significantly in risk factor. Some can kill more than 30% of those infected (such as MERS-CoV), and some are relatively harmless, such as the common cold. Coronaviruses cause colds with major symptoms, such as fever, and sore throat from swollen adenoids, occurring primarily in the winter and early spring seasons. Coronaviruses can cause pneumonia (either direct viral pneumonia or a secondary bacterial pneumonia) and bronchitis (either direct viral bronchitis or a secondary bacterial bronchitis). The much publicized human coronavirus discovered in 2003, SARS-CoV, which causes severe acute respiratory syndrome (SARS), has a unique pathogenesis because it causes both upper and lower respiratory tract infections.

Seven strains of human coronaviruses are known, of which four produce the generally mild symptoms of the common cold:

1. Human coronavirus OC43 (HCoV-OC43)
2. Human coronavirus HKU1
3. Human coronavirus NL63 (HCoV-NL63, New Haven coronavirus)
4. Human coronavirus 229E (HCoV-229E)

– and three, symptoms that are potentially severe:

1. Middle East respiratory syndrome-related coronavirus (MERS-CoV), previously known as *novel coronavirus 2012* and *HCoV-EMC*
2. Severe acute respiratory syndrome coronavirus (SARS-CoV or "SARS-classic")
3. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), previously known as 2019-nCoV or "novel coronavirus 2019"

The coronaviruses HCoV-229E, -NL63, -OC43, and -HKU1 continually circulate in the human population and cause respiratory infections in adults and children world-wide.

Outbreaks of coronavirus types of relatively high mortality are as follows:

Outbreak	Virus type	Deaths
2003 severe acute respiratory syndrome outbreak	SARS-CoV	774[40]
2012 Middle East respiratory syndrome coronavirus outbreak	MERS-CoV	Over 400[41]
2015 Middle East respiratory syndrome outbreak in South Korea	MERS-CoV	36[42]
2018 Middle East respiratory syndrome outbreak	MERS-CoV	41[43]
2019–2020 coronavirus pandemic	SARS-CoV- 2	At least 14,641[44]

Replication

It is thought that human coronaviruses enter cells, predominantly, by specific receptors. Aminopeptidase-N and a sialic acid-containing receptor have been identified to act in such a role for 229E and OC43 respectively. After the virus enters the host cell and uncoats, the genome is transcribed and then translated. A unique feature of replication is that all the mRNAs form a "nested set" with common 3′ ends; only the unique portions of the 5′ ends are translated. There are 7 mRNAs produced. The shortest mRNA codes for the nucleoprotein, and the others each direct the synthesis of a further segment of the genome. The proteins are assembled at the cell membrane and genomic RNA is incorporated as the mature particle forms by budding from internal cell membranes.

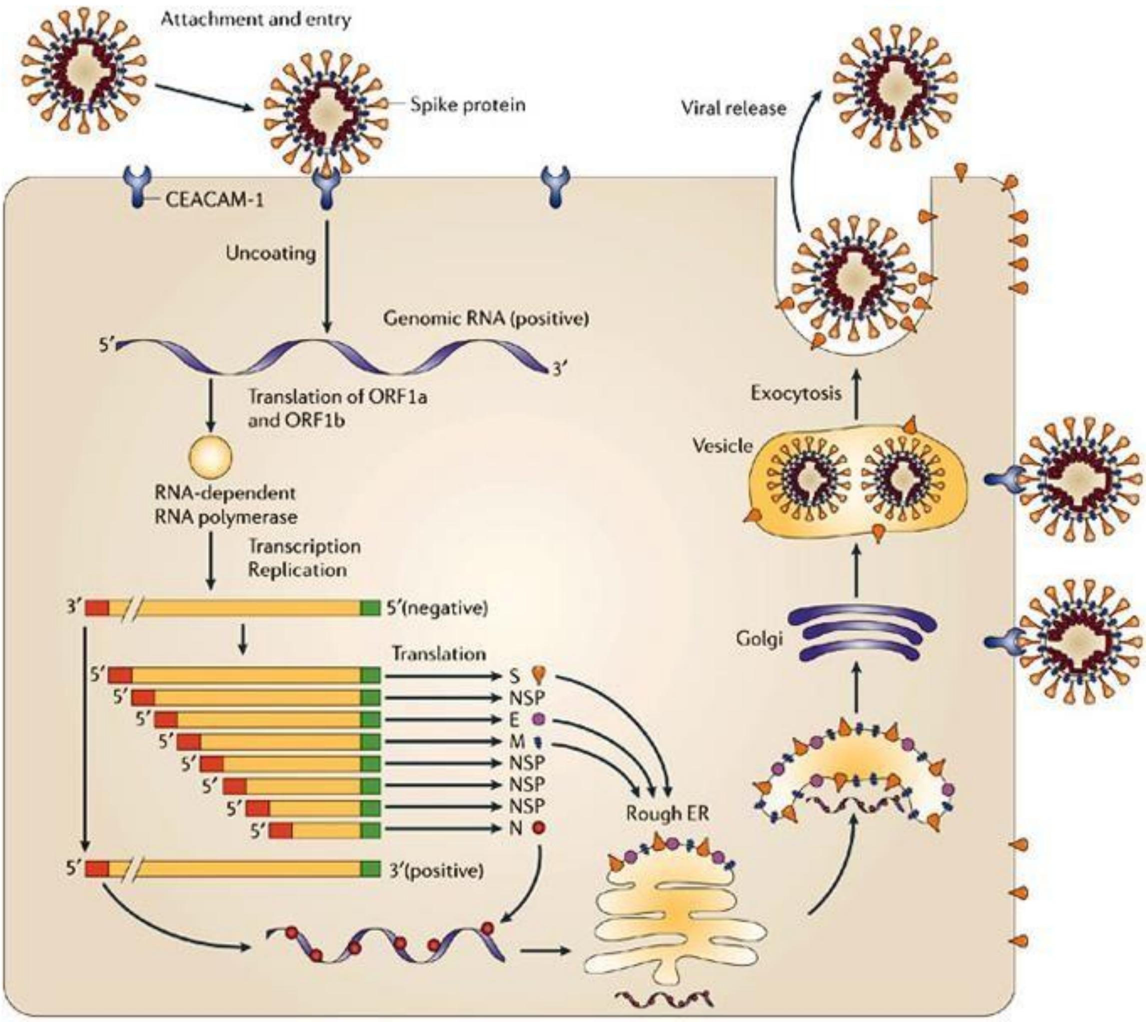
Coronaviruses are large, enveloped RNA viruses of both medical and veterinary importance. Interest in this viral family has intensified in the past few years as a result of the identification of a newly emerged coronavirus as the causative agent of severe acute respiratory syndrome (SARS). At the molecular level, coronaviruses employ a variety of unusual strategies to accomplish a complex program of gene expression. Coronavirus replication entails ribosome frameshifting during genome translation, the synthesis of both genomic and multiple subgenomic RNA species, and the assembly of progeny virions by a pathway that is unique among enveloped RNA viruses. Progress in the investigation of these processes has been enhanced by the development of reverse genetic systems, an advance that was heretofore obstructed by the enormous size of the coronavirus genome.

The hallmark of coronavirus transcription is the production of multiple subgenomic mRNAs that contain sequences corresponding to both ends of the genome. (Transcription is defined as the process whereby subgenome-sized mRNAs are produced, and coronavirus replication is the process whereby genome-sized RNA, which also functions as mRNA, is produced.) Thus, the generation of subgenomic mRNAs involves a process of discontinuous transcription.

The coronavirus genomic RNA of approximately 30,000 nucleotides encodes structural proteins of the virus, nonstructural proteins that have a critical role in viral RNA synthesis (which we will refer to as replicase-transcriptase proteins), and nonstructural proteins that are nonessential for virus replication in cell culture but appear to confer a selective advantage in vivo (which we will refer to as niche-specific proteins). At least one niche-specific protein, nonstructural protein 2 (nsp2), and one structural protein, the nucleocapsid protein (N), are involved in viral RNA synthesis.

The expression of the coronavirus replicase-transcriptase protein genes is mediated by the translation of the genomic RNA. The replicase-transcriptase proteins are encoded in open- reading frame 1a (ORF1a) and ORF1b and are synthesized initially as two large polyproteins, pp1a and pp1ab. The synthesis of pp1ab involves programmed ribosomal frame shifting during translation of ORF1a. During or after synthesis, these polyproteins are cleaved by virus- encoded proteinases with papain-like (PLpro) and chymotrypsin-like folds into 16 proteins; nsp1 to nsp11 are encoded in ORF1a, and nsp12 to nsp16 are encoded in ORF1b. The replicase-transcriptase proteins, together with other viral proteins and, possibly, cellular proteins, assemble into membrane-bound replication-transcription complexes (RTC). (We will use the term RTC to describe complexes copying or producing genome- or subgenome-length RNA.) These complexes accumulate at perinuclear regions and are associated withdouble-membrane vesicles. Hydrophobic transmembrane domains are present in nsp3, nsp4, and nsp6 and likely serve to anchor the nascent pp1a/pp1ab polyproteins to membranes during the first step of RTC formation.

The mechanism of coronavirus replication hereby will take the coronavirus replication of MHV (mouse hepatitis virus) for example.



Summary of mouse hepatitis virus (MHV) replication. MHV binds to the host-cell receptor CEACAM-1 through interaction of the spike (S) glycoprotein. Virus entry into the host cell can occur through fusion with the surface of the host cell, with the subsequent release of the genomic RNA into the cytoplasm. Alternatively, MHV can enter the host cell through the formation of endocytic vesicles, and genomic RNA is released into the cytoplasm following fusion with the vesicle membrane (not shown). Translation of the positive-strand genomic RNA gives rise to a large polyprotein that undergoes proteolytic processing to generate an RNA-dependent RNA polymerase. Through the action of the RNA polymerase, a full-length, antisense negative-strand template is generated. Subgenomic mRNAs are synthesized, presumably from subgenomic negative-strand templates. Translation of subgenomic mRNAs gives rise to structural viral proteins. S glycoprotein is expressed on the surface of the host cell and this might contribute to fusion with neighbouring uninfected cells by binding to CEACAM- 1. Virus assembly occurs within vesicles, followed by virus release by fusion of virion- containing vesicles with the plasma membrane. Released virus can infect other cells and can replicate within the parent cell through binding to CEACAM-1. E, envelope protein; ER, endoplasmic reticulum; M, membrane protein; N, nucleocapsid protein; ORF, open reading frame.

Pathogenesis

Studies in both organ cultures and human volunteers show that coronaviruses are extremely fastidious and grow only in differentiated respiratory epithelial cells. Infected cells become vacuolated, show damaged cilia, and may form syncytia. Cell damage triggers the production of inflammatory mediators, which increase nasal secretion and cause local inflammation and swelling. These responses in turn stimulate sneezing, obstruct the airway, and raise the temperature of the mucosa.

Epidemiology

The epidemiology of coronavirus colds has been little studied. Waves of infection pass through communities during the winter months, and often cause small outbreaks in families, schools, etc. Immunity does not persist, and subjects may be re-infected, sometimes within a year. The pattern thus differs from that of rhinovirus infections, which peak in the fall and spring and generally elicit long-lasting immunity. About one in five colds is due to corona viruses.

The rate of transmission of coronavirus infections has not been studied in detail. The virus is usually transmitted via inhalation of contaminated droplets, but it may also be transmitted by the hands to the mucosa of the nose or eyes.

Diagnosis

There is no reliable clinical method to distinguish coronavirus colds from colds caused by rhinoviruses or less common agents. For research purposes, virus can be cultured from nasal swabs or washings by inoculating organ cultures of human fetal or nasal tracheal epithelium. The virus in these cultures is detected by electron microscopy or other methods. The most useful method for laboratory diagnosis is to collect paired sera (from the acute and convalescent phases of the disease) and to test by ELISA for a rise in antibodies against OC43 and 229E. Complement fixation tests are insensitive; other tests are inconvenient and can be used only for one serotype. Direct hybridization and polymerase chain reaction tests for viral nucleic acid have been developed and, particularly with the latter, are the most sensitive assays currently available for detecting virus.

12 Facts showing symptoms of coronavirus

The COVID-19 infection has been declared a pandemic which has led to worldwide lockdowns and an overall state of panic and fear. We have now reached more than 200,000 cases worldwide. The virus presents itself with flu-like symptoms that include fever and dry cough. As doctors around the world are still grappling with finding a cure for the novel coronavirus, here is a list of twelve symptoms as explained by survivors of the pandemic.

1. Painful sinuses

Painful sinuses are common with the flu and the cold. It can be very painful and often paired with a dull pressure. Connor Reed, a resident of Wuhan city in China, said that the sinuses were agonizing. Reed contracted the virus in November 2019 making him one of the first people to contract the strain of the novel coronavirus. "I ache all over, my head is thumping, my eyes are burning, my throat is constricted," he wrote in his diary.

2. Ear pressure

Connor discovered that his ears made him feel that they were ready to pop. It is most likely to be caused by clogged up ears because of the virus. The Eustachian tube, leading between the inner and the middle ear, becomes clogged and that can cause you to feel pressure in your ears. It is advisable not to use an earbud to massage and help relieve the pressure. That can cause more harm than good.

3. Thumping headache

A headache is common when you have the flu or the cold. It can also be caused by dehydration. Do not panic the moment you start experiencing a headache. People suffering from coronavirus are advised to take paracetamol instead of an ibuprofen whenever required. Kevin Harris was admitted to a hospital Ohio recounts that the worst part was the pain. He said that on a scale of 10, the pain was a 15.

4. Burning eyes

The sensation of burning in the eye's mimics to the irritation and itchiness that you face during other allergies. Such irritation can also be caused by smoke, smog and other allergens. Connor Reed also recorded that the symptoms that initially felt like the flu had no worsened and caused his eyes to burn and he developed a headache.

5. Constricted throat

A constricted throat can be caused by inflammation of the throat caused by continuous coughing which is a characteristic symptom of the disease. If you are having trouble breathing or swallowing, it is important that you see a doctor immediately. Andrew O' Dwyer caught the infection in Italy. He said that the cough was quite debilitating. "The worst bit was the uncontrollable coughing," he said.

6. Body aches

People with coronavirus experience severe pain in their body. It is not restricted to the ears and the chest but also the arm and legs. This can be due to the fever that occurs during coronavirus infection. The stress and tension also add to the aches. Elizabeth Schneider, a resident of Seattle, said that the first symptoms she experienced were severe headaches, body and joint aches along with a very high fever.

7. Lungs sound like a paper bag

If your lung sounds crackly when you breathe, it could be symptoms of pneumonia. The crackly breathing can be caused by fluids in your air sacs which is linked to the coronavirus infection. Marc Thibault, from Rhode Island, said he felt as if he is as asphyxiating and panicked because he could not breathe.

8. Fatigue and lack of appetite

Fatigue is a common symptom during the flu. It is advisable to rest as much as you can at times like these. Jaimuay Sae-Ung, the first Thai citizen to contract the virus, recounts that she was always tired, fatigued and couldn't eat. She also complained she never felt up to eating while she had coronavirus.

9. Fever

Fever was discovered to be one of the first symptoms to be identified. People thought that a fever is the only symptom for the virus infection. Many patients only experienced a fever without the onset of any respiratory problems or cough. Rohit Dutta, Delhi's first COVID-19 patient said he experienced a fever on the day when he returned from his trip to Italy and then again after a few days. This is when he got himself tested and was found to be positive for the coronavirus infection.

10. Tightness in the chest

Along with a fever, the first symptoms to be discovered were tightness and persistent coughs. The virus also spreads through respiratory droplets from the coughs. Therefore it is advised to cough and sneeze on a flexed elbow. Carl Goldman from Santa Clarita, who was aboard the Diamond Princess, said that he developed a fever and 'a bit of a cough' during his flight back to America and was quarantined on his return. His chest feels tight and had coughing spells.

11. Jet Lag

Fridget Wilkins, who lives in London, started experiencing symptoms after she returned from Australia. She felt tired and sore, which she thought was because of jet lag. Just like fatigue, the feeling of jet lag can make people feel that they're not quite up to it.

12. Feeling like passing out

The virus can have a toll on the patient and leave them drained and always feeling like they are about to pass out. David and Sally Abel, from Oxfordshire, recorded their journey of battling with their infection. They, too, like many others felt the same when they were tested positive.

Control

Infection prevention and control during health care when novel coronavirus (nCoV) infection is suspected

This is the first edition of guidance on infection prevention and control (IPC) strategies for use when infection with a novel coronavirus (2019-nCoV) is suspected. It has been adapted from WHO's Infection prevention and control during health care for probable or confirmed cases of Middle East respiratory syndrome coronavirus (MERS-CoV) infection, based on current knowledge of the situation in China and other countries where cases were identified and experiences with severe acute respiratory syndrome (SARS)-CoV and MERS-CoV.

Advice on the Use of Masks

This document provides rapid advice on the use of medical masks in communities, at home and at health care facilities in areas that have reported outbreaks caused by the 2019 novel coronavirus (nCoV). It is intended for public health and infection prevention and control (IPC) professionals, health care managers, health care workers and community health workers.

Home care for patients with suspected novel coronavirus (nCoV) infection presenting with mild symptoms and management of contacts.

WHO has developed this rapid advice note to meet the need for recommendations on the safe home care for patients with suspected novel coronavirus (2019-nCoV) infection presenting with mild symptoms and public health measures related to management of asymptomatic contacts.

Q&A on infection prevention and control for health care workers caring for patients with suspected or confirmed 2019-nCoV.

Are boots, impermeable aprons, or coverall suits required as routine person protective equipment (PPE) for healthcare workers (HCW) caring for patients with suspected or confirmed 2019-nCoV infection? Can disposable medical face masks be sterilized and reused? Do patients with suspected or confirmed 2019-nCoV need to be hospitalized if they have mild illness? Here you will find answers to these and other questions related to infection prevention and control for health care workers caring for patients with suspected or confirmed 2019-nCoV.

Water, sanitation, hygiene and waste management for COVID-19.

This Technical Brief supplements existing IPC documents by referring to and summarizing WHO guidance on water, sanitation and health care waste which is relevant for viruses (including coronaviruses). This Technical Brief is written in particular for water and sanitation practitioners and providers.

Guide to local production of WHO-recommended Handrub Formulations
Part A provides a practical guide for use at the pharmacy bench during the actual preparation of the formulation. Users may want to display the material on the wall of the production unit. Part B summarizes some essential background technical information and is taken from WHO Guidelines on Hand Hygiene in Health Care (2009). Within Part B the user has access to important safety and cost information and supplementary material relating to dispensers and distribution.

Key Messages and Actions for COVID-19 Prevention and Control in Schools
The purpose of this document is to provide clear and actionable guidance for safe operations through the prevention, early detection and control of COVID-19 in schools and other educational facilities. The guidance, while specific to countries that have already confirmed the transmission of COVID-19, is still relevant in all other contexts. Education can encourage students to become advocates for disease prevention and control at home, in school, and in their community by talking to others about how to prevent the spread of viruses. Maintaining safe school operations or reopening schools after a closure requires many considerations but, if done well, can promote public health.

Getting your workplace ready for COVID-19
WHO and public health authorities around the world are taking action to contain the COVID- 19 outbreak. However, long term success cannot be taken for granted. All sections of our society – including businesses and employers – must play a role if we are to stop the spread of this disease.

IPC guidance for long-term care facilities in the context of COVID-19
The objective of this interim guidance is to provide guidance on Infection Prevention and Control in Long-Term Care Facilities (LTCF) in the context of COVID-19 to prevent COVID- 19-virus from entering the facility, spreading within the facility, and spreading to outside the facility. This guidance is for LTCF managers and corresponding IPC focal persons in LTCF.

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