



What Is a Coronavirus?

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COVID-19 Actuaries Response Group - Learn. Share. Educate. Influence.

Introduction

Coronaviruses are a family of hundreds of viruses known for containing strains that cause potentially deadly diseases in mammals and birds. In humans they're typically spread via airborne droplets of fluid produced by infected individuals. Coronaviruses are believed to cause a significant proportion of all common colds in adults and children.

In humans, this virus can cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). (WHO, 2020)

After the virus has entered its host's cells, the virus particle is uncoated and its genome enters the cell cytoplasm, encoding a protein allowing the viral genome to be transcribed into new RNA copies using the host cell's machinery.

A viral infection does not always cause disease. A viral infection simply involves viral replication in the host, but disease is the damage caused by the viral multiplication. Damage to the human body occurs when viral replication produces factors that interfere with host cellular processes resulting in cell death.

Coronaviruses are transmitted between animals and people. Previous research found that SARS-CoV was transmitted from civet cats to humans and MERS-CoV from dromedary camels to humans. Several known coronaviruses are circulating in animals that have not yet infected humans.

Coronaviruses are enveloped viruses with a positive-sense single-stranded RNA genome and a nucleocapsid of helical symmetry. The name coronavirus is derived from the Latin *corona*, meaning 'crown' or 'halo', referring to the characteristic appearance of the virus particles (virions): they have a fringe reminiscent of a crown or of a solar corona. Proteins that contribute to the overall structure of all coronaviruses are the spike (S), envelope (E), membrane (M), and nucleocapsid (N).

Coronaviruses are divided into four genera: alpha, beta, gamma, and delta; gamma and delta coronaviruses mostly infect birds, while alpha and beta mostly reside in mammals.

Human coronaviruses were first identified in the mid-1960s. The seven coronaviruses that can infect people are:

- 229E (alpha coronavirus)
- NL63 (alpha coronavirus)
- OC43 (beta coronavirus)
- HKU1 (beta coronavirus)
- MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)
- SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS)
- 2019 Novel Coronavirus (SARS-CoV2) (ECDC, 2020)

The coronaviruses HCoV-229E, -NL63, -OC43, and -HKU1 continually circulate in the human population and cause respiratory infections in adults and children worldwide. (Corman et al, 2018)

SARS-CoV-2

On 29 December 2019, Chinese authorities identified a cluster of similar pneumonia cases of unknown aetiology in Wuhan City, Hubei Province, China. A novel strain of coronavirus (2019-nCoV) was subsequently isolated from a patient on the 7th of January 2020. Most cases from the initial cluster had epidemiological links with a live animal market (Huanan South China Seafood Market), suggesting a possible zoonotic origin.

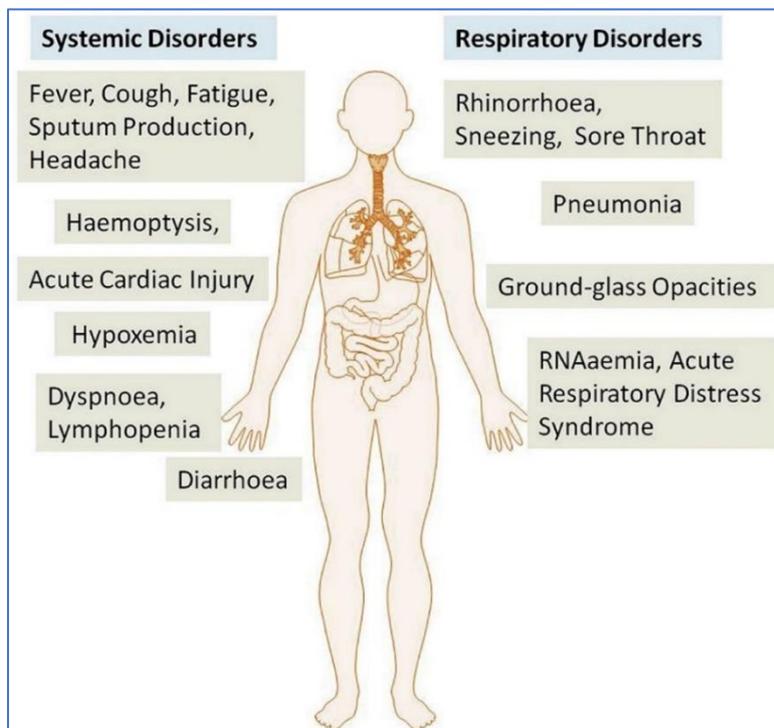
On the 30th of January 2020, the World Health Organization (WHO) declared the emergence of this novel coronavirus (2019-nCoV) a public health emergency of international concern (PHEIC). This decision by WHO Director-General (DG) Tedros Adhanom Ghebreyesus, was made following the recommendations of the Emergency Committee in its second meeting convened under the International Health Regulations (IHR). On the 11th of March 2020, the epidemic was declared a pandemic.

As an RNA virus, SARS-CoV-2 still has the inherent feature of a high mutation rate, although like other coronaviruses the mutation rate might be somewhat lower than other RNA viruses because of its genome-encoded exonuclease. (Wang C *et al*, 2020)

COVID-19

COVID-19 is the name given for the disease caused by SARS-CoV-2.

The figure below displays the systemic and respiratory disorders caused by infection with SARS-CoV-2. COVID-19 shows some unique clinical features compared to previous coronavirus infections that include the targeting of the lower airway as evidenced by upper respiratory tract symptoms like rhinorrhoea, sneezing, and sore throat. Additionally, patients infected with SARS-CoV-2 develop intestinal symptoms like diarrhoea while only a low percentage of MERS-CoV or SARS-CoV patients experienced diarrhoea.



(Rothan & Byrareddy, 2020)

Immune Response

The human immune system subsequently responds through initiation of the inflammatory response; however, this can on occasion cause more damage due to an overly vigorous immune reaction. Cytokines are proteins used by the immune system and in an unregulated immune response, there can be a surge of activated immune cells into the lungs (a 'cytokine storm'). The resulting lung inflammation and fluid build-up can lead to respiratory distress and can be contaminated by a secondary bacterial pneumonia – often increasing mortality.

ARDS

In some of the most severe COVID-19 cases, the cytokine response – combined with a diminished capacity to adequately oxygenate the body – can result in multi-organ failure. Patients with severe illness may develop dyspnea and hypoxemia within one week of onset of the disease, which may quickly progress to acute respiratory distress syndrome (ARDS) or end-organ failure.

Disease Course

There seem to be two main stages of illness that patients may move through.

- *Replicative stage* – Viral replication occurs over a period of several days. An innate immune response occurs, but this response fails to contain the virus. Relatively mild symptoms may occur due to direct viral cytopathic effect and innate immune responses.
- *Adaptive immunity stage* – An adaptive immune response eventually kicks into gear. This leads to falling titres of virus. However, it may also increase levels of inflammatory cytokines and lead to tissue damage – causing clinical deterioration.

This progression may explain the clinical phenomenon whereby patients seem fairly normal for several days, but then suddenly deteriorate when they enter the adaptive immunity stage. (*Kings College Hospital, 2020*)

Comorbidities

Existing comorbidities place patients at higher risk of developing ARDS, and then progression to death. In addition, older age is associated with greater risk of development of ARDS and death likely owing to less rigorous immune response. (*Wu et al, 2020*)

| Features | Hazard Ratio (95%CI) | P Value |
|--------------------------------|----------------------|---------|
| Type of comorbidities | | |
| COPD | 2.681 (1.424-5.048) | 0.002 |
| Diabetes | 1.586 (1.028-2.449) | 0.037 |
| Hypertension | 1.575 (1.069-2.322) | 0.022 |
| Malignant tumor | 3.501 (1.604-7.643) | 0.002 |
| Number of comorbidities | | |
| 1 | 1.789 (1.155-2.772) | 0.009 |
| 2 or more | 2.592 (1.611-4.171) | <0.001 |

In studies of ARDS survivors, long-term mortality has been reported to range between 11 and 60%, not dependent on the severity of ARDS but mainly on age and comorbidities. A reduced quality of life characterized by persistent exercise limitations and neuropsychological disorders may persist with a potential for development of pulmonary fibrosis.

As previously mentioned, comorbidities play a crucial role in patient survival and their effect on clinical outcomes has been studied. The table above displays the mortality hazard ratios derived from analysis of 1,590 laboratory-confirmed hospitalized patients in China (*Guan et al, 2020*).

In addition, patients with two or more comorbidities had significantly increased mortality risks.

Management of a pandemic is reliant on a number of key strands including surveillance. Tracking the pandemic provides the core information on which pandemic response decisions are made. In addition, and crucial in how well we can respond, is healthcare infrastructure. When estimating potential mortality from a pandemic, healthcare capacity is an important datapoint; but ultimately, is central to government decisions and reducing mortality.

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