

WHAT CAUSES COVID-19?

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A VIRUS CAUSES COVID-19, SO WHAT IS A VIRUS?

A virus is a tiny particle, so small that it cannot be seen with a light microscope, but must be observed with an electron microscope. A virus particle, or virion, consists of the following:

- **Nucleic acid** – set of genetic instructions, either DNA or RNA, either single-stranded or double-stranded
- **Coat (or capsid) of protein** – surrounds the DNA or RNA to protect it
- **Lipid membrane** – surrounds the protein coat (found only in some viruses, including influenza; these types of viruses are called **enveloped** viruses as opposed to naked viruses)

Viruses vary widely in their shape and complexity. Unlike bacteria, viruses don't contain the chemical machinery (enzymes) needed to carry out the chemical reactions for life. So, a virus must have a **host cell** (bacteria, plant or animal) in which to live and make more viruses. Outside of a host cell, viruses cannot function.

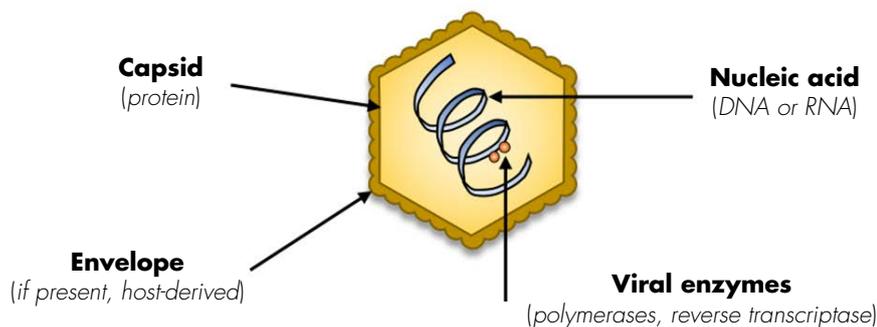


Diagram of a typical virus

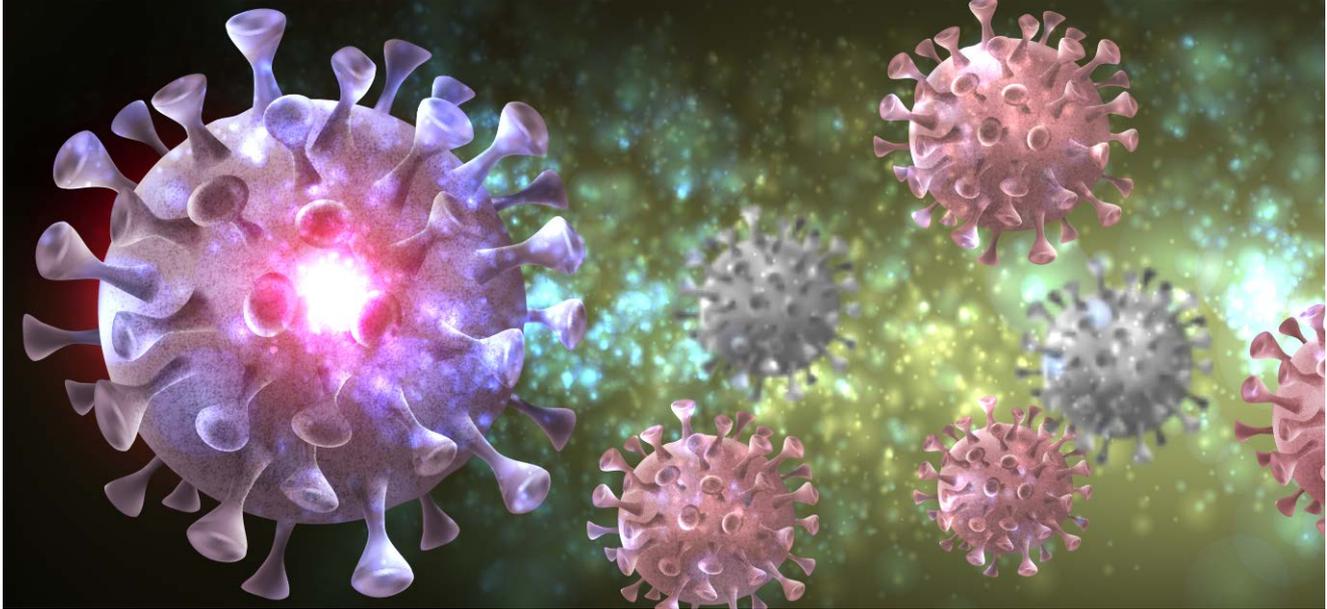
WHAT IS THE SPECIFIC VIRUS THAT CAUSES COVID-19?

The official name for the virus that causes COVID-19 was announced by the International Committee on Taxonomy of Viruses (ICTV) on 11 February 2020 as "**severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)**". Viruses are named based on their genetic structure to help facilitate the development of diagnostic tests, vaccines and treatments. SARS-CoV-2 was chosen because it is genetically related to the coronavirus responsible for the SARS outbreak of 2003.

Viruses and the diseases they cause, often have different names eg HIV is the virus that causes AIDS & SARS-CoV-2 is the virus that causes COVID-19

WHAT ARE CORONAVIRUSES AND HOW MANY ARE THERE?

Under an electron microscope coronavirus particles usually appear spherical, have a lipid outer envelope, with a crown of club-shaped spikes on their surface. The name “coronavirus” is derived from the Greek **κορώνα**, meaning crown. Using molecular methods, coronaviruses are classified as positive-sense, single-stranded RNA viruses: coronaviruses have extraordinarily large single-stranded RNA genomes – approximately 26,000 to 32,000 bases or RNA “letters” in length.



Coronavirus (licensed from ecco/stock.adobe.com)

‘Why is the fact it is a positive-sense, single stranded RNA virus important? They have genetic material that can function both as a genome and as messenger RNA; it can be directly translated into protein in the host cell. The first proteins to be expressed after infection serve genome replication functions. Therefore antivirals which specifically inhibit RNA replication may be of benefit’

Scientists have divided the family of coronaviruses into **four sub-groupings or genera**. Coronaviruses are ecologically diverse with the greatest variety seen in bats, suggesting that they are the **main hosts** for many of these viruses. Mammals that live in or around humans such as bats, hens, and rats may serve as intermediate hosts, the viruses can mutate (change) in them which may result in the virus then being able to infect humans – this is referred to as zoonotic transmission. The surface spike (S) glycoprotein is critical for binding of **host cell receptors** and is believed to represent the key to determining whether a virus will infect a particular host.

Alpha		18 coronaviruses 2 can infect humans (229E & NL63)	<ul style="list-style-type: none"> Alpha – 18 coronaviruses, 2 can infect humans (229E & NL63)
Beta		14 coronaviruses 5 can infect humans (OC43, HKU1, MERS-CoV, SARS-CoV & SARS-CoV-2)	<ul style="list-style-type: none"> Beta – 14 coronaviruses, 5 can infect humans (OC43, HKU1, MERS-CoV, SARS-CoV & SARS-CoV-2)
Gamma		5 coronaviruses	<ul style="list-style-type: none"> Gamma – 5 coronaviruses
Delta		7 coronaviruses	<ul style="list-style-type: none"> Delta – 7 coronaviruses

Types of coronavirus

The four common coronaviruses that infect humans are: 229E; NL63; OC43; HKU1. These cause **10 to 30% of upper respiratory tract infections**, such as the common cold in adults. The three less common and more severe pathogenic human beta-coronaviruses are:

- MERS-CoV, which causes Middle East respiratory syndrome (MERS)
- SARS-CoV, which causes severe acute respiratory syndrome (SARS)
- SARS-CoV-2, which causes COVID-19.

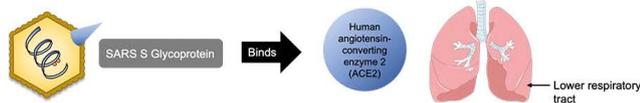
WHAT CAN WE LEARN FROM OTHER SEVERE CORONAVIRUSES?

SARS-CoV first emerged in 2002 in Guangdong, China as an unusual pneumonia, which developed into life-threatening respiratory failure in certain cases. The virus rapidly spread across 29 countries, infecting more than 8000 people and killing about 800. Because early cases shared a history of human-animal contact at live game markets, zoonotic transmission of the virus was strongly suspected, and the consensus now is that bats were the natural hosts. Human-to-human transmission was documented, mostly in health care settings. See the schematic below for an outline of why this virus is different to the common cold and why it was mainly transmitted in the hospital, although several mini-outbreaks did occur in the community.

‘All the severe coronavirus diseases are thought to be caused initially by zoonotic transmission which is where the virus has jumped from non-human animals to humans’

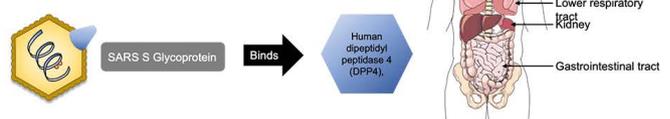
The MERS-CoV epidemic appeared in Saudi Arabia in 2012, with people experiencing similar symptoms to SARS-CoV but dying at a much higher rate. Unlike SARS-CoV, which spread quickly and widely, MERS-CoV has been mainly limited to Saudi Arabia. MERS-CoV has not yet sustained community spread; instead, it has caused large nosocomial (in-hospital) transmission events, in some cases linked to a single super-spreader. The natural host of MERS-CoV is presumed to be bats, yet human transmission events have primarily been attributed to an intermediate host, the dromedary camel. Patients with MERS have prominent gastrointestinal symptoms and often acute kidney failure, as a result of a different receptor for the spike protein.

SARS-CoV caused SARS (predominantly spread in hospitals)



Viral shedding occurred late (~10 days) in illness when individuals were already hospitalized

MERS-CoV caused MERS



SARS and MERS were caused by different coronavirus variants binding to different receptors in the human body

A **recent study in a nonhuman primate model** (cynomolgus macaques) has shown that SARS-CoV-2, was detected in the mucous from the nasal chamber as early as four days after inoculation, and this was not seen either in the case of SARS-CoV (on the same animals) or MERS-CoV. The early shedding of the SARS-CoV-2 virus is quite similar to the influenza virus. This is of serious concern as early shedding may explain why detection and isolation may not be very effective for containing SARS-CoV-2. They also found that productive infection took place without any overt clinical signs, i.e. asymptomatic cases. The researchers also found that SARS-CoV-2 RNA was present in organs other than respiratory tract like the intestine, though it is thought this is not a primary means of transmission.

Many of the early cases of COVID-19 were traced back to a large seafood and animal market in Wuhan. The virus is thought to have come from bats, possibly via an intermediary animal. In response, Chinese officials enacted a **ban on eating and trading wildlife** in February.