Coronavirus: General Properties and Diseases

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Introduction

Coronaviruses are a group of related RNA viruses that cause diseases in mammals and birds. In humans and birds, they cause respiratory tract infections that can range from mild to lethal. Mild illnesses in humans include some cases of the common cold (which is also caused by other viruses, predominantly rhinoviruses). More lethal varieties of the virus can cause SARS, MERS and COVID-19, which is causing the ongoing pandemic. In cows and pigs, they cause diarrhea, while in mice they cause hepatitis and encephalomyelitis.

General Properties

Basic Structure

- **Enveloped viruses** with a positive-sense single-stranded RNA genome
- **Nucleocapsid** of helical symmetry
- **Genome size** ranges from approximately 26 to 32 kilobases, one of the largest among RNA viruses
- **Characteristic club-shaped spikes** that project from their surface, which in electron micrographs create an image reminiscent of the stellar corona, from which their name derives

Physical Characteristics

- **Large, roughly spherical particles** with unique surface projections
- **Size is highly variable** with average diameters of 80 to 120 nm
- **Extreme sizes** are known from 50 to 200 nm in diameter
- **Enclosed in an envelope** embedded with a number of protein molecules
- The **lipid bilayer envelope**, membrane proteins, and nucleocapsid protect the virus when it is outside the host cell

Structural Proteins

Membrane Proteins

- **Membrane (M)**, **envelope (E)** and **spike (S)** structural proteins are anchored in the viral envelope
- **E and M proteins** are the structural proteins that combined with the lipid bilayer to shape the viral envelope and maintain its size

Spike Proteins

- **S proteins** are needed for interaction of the virus (receptor binding and membrane fusion) with the host cells
- **Exception:** Human coronavirus NL63 is peculiar in that its M protein has the binding site for the host cell, and not its S protein
- The **spikes are the most distinguishing feature** of coronaviruses and are responsible for the corona- or halo-like surface
- On average a coronavirus particle has **74 surface spikes**
- Each spike is about **20 nm long** and is composed of a trimer of the S protein
- **S1 proteins** are the most critical components in terms of infection and are also the most variable components as they are responsible for host cell specificity

Additional Proteins

- A subset of coronaviruses (specifically the members of betacoronavirus subgroup A) also has a shorter spike-like surface protein called **hemagglutinin esterase (HE)** which help in the attachment to and detachment from the host cell

Nucleocapsid

- Inside the envelope, there is the **nucleocapsid**, which is formed from multiple copies of the nucleocapsid (N) protein
- These are bound to the positive-sense single-stranded RNA genome in a continuous **beads-on-a-string type conformation**

Transmission

General Transmission Mechanisms

- **Infected carriers** are able to shed viruses into the environment
- The interaction of the coronavirus spike protein with its complementary cell receptor is central in determining the **tissue tropism**, **infectivity**, and **species range** of the released virus
- Coronaviruses mainly target **epithelial cells**
- They are transmitted from one host to another host, depending on the coronavirus species, by either an **aerosol**, **fomite**, or **fecal-oral route**

Host-Specific Transmission

- **Human coronaviruses** infect the epithelial cells of the respiratory tract
- **Animal coronaviruses** generally infect the epithelial cells of the digestive tract

Specific Examples

- **SARS coronavirus** infects the human epithelial cells of the lungs via an aerosol route by binding to the angiotensin-converting enzyme 2 (ACE2) receptor
- **Transmissible gastroenteritis coronavirus (TGEV)** infects the pig epithelial cells of the digestive tract via a fecal-oral route

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Classification of Coronaviruses

Taxonomic Hierarchy

Coronaviruses form the subfamily **Orthocoronavirinae** which is one of two subfamilies in the family **Coronaviridae**, order **Nidovirales**, and realm **Riboviria**.

Four Genera

1. **Alphacoronavirus**
2. **Betacoronavirus**
3. **Gammacoronavirus**
4. **Deltacoronavirus**

Host Specificity

- **Alphacoronaviruses and betacoronaviruses** infect mammals
- **Gammacoronaviruses and deltacoronaviruses** primarily infect birds

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Origin of Coronaviruses

Natural Reservoirs

- **Bats and birds**, as warm-blooded flying vertebrates, are an ideal natural reservoir for the coronavirus gene pool
- **Bats** are the reservoir for alphacoronaviruses and betacoronavirus
- **Birds** are the reservoir for gammacoronaviruses and deltacoronaviruses
- The large number and global range of bat and avian species that host viruses have enabled extensive evolution and dissemination of coronaviruses

Evolution Timeline

- The human coronavirus **NL63** shared a common ancestor with a bat coronavirus (ARCoV.2) between **1190 and 1449 CE**
- **Alpaca coronavirus** and **human coronavirus 229E** diverged sometime before **1960**
- **MERS-CoV** emerged in humans from bats through the intermediate host of camels
- The most closely related bat coronavirus and **SARS-CoV** diverged in **1986**

- The ancestors of SARS-CoV first infected leaf-nose bats of the genus; subsequently, they spread to horseshoe bats in the species Rhinolophidae, then to Asian palm civets, and finally to humans

Bovine Coronavirus Origin

- Unlike other betacoronaviruses, **bovine coronavirus** of the species Betacoronavirus 1 and subgenus Embecovirus is thought to have originated in **rodents** and not in bats
- In the **1790s**, equine coronavirus diverged from the bovine coronavirus after a cross-species jump
- Later in the **1890s**, human coronavirus OC43 diverged from bovine coronavirus after another cross-species spillover event
- It is speculated that the **flu pandemic of 1890** may have been caused by this spillover event, and not by the influenza virus, because of the related timing, neurological symptoms, and unknown causative agent of the pandemic

Neurological Implications

- Besides causing respiratory infections, human coronavirus **OC43** is also suspected of playing a role in neurological diseases
- In the **1950s**, the human coronavirus OC43 began to diverge into its present genotypes
- Phylogenetically, **mouse hepatitis virus** (Murine coronavirus), which infects the mouse's liver and central nervous system, is related to human coronavirus OC43 and bovine coronavirus
- Human coronavirus **HKU1**, like the aforementioned viruses, also has its origins in rodents

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Infection in Humans

Risk Variability

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.

Symptoms and Complications

- Coronaviruses can cause colds with major symptoms, such as **fever**, and a **sore throat** from swollen adenoids
- Coronaviruses can cause **pneumonia** (either direct viral pneumonia or secondary bacterial pneumonia)
- They can cause **bronchitis** (either direct viral bronchitis or secondary bacterial bronchitis)
- The 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

Human Coronavirus Species

Seven Strains Total

Six species of human coronaviruses are known, with one species subdivided into two different strains, making **seven strains** of human coronaviruses altogether.

Four Mild Strains

Four human coronaviruses produce symptoms that are generally mild, even though it is contended they might have been more aggressive in the past:

1. **Human coronavirus OC43 (HCoV-OC43)**, β-CoV
2. **Human coronavirus HKU1 (HCoV-HKU1)**, β-CoV
3. **Human coronavirus 229E (HCoV-229E)**, α-CoV
4. **Human coronavirus NL63 (HCoV-NL63)**, α-CoV

Three Severe Strains

Three human coronaviruses produce potentially severe symptoms:

1. **Severe acute respiratory syndrome coronavirus (SARS-CoV)**, β-CoV (identified in 2003)
2. **Middle East respiratory syndrome-related coronavirus (MERS-CoV)**, β-CoV (identified in 2012)
3. **Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)**, β-CoV (identified in 2019)

These cause the diseases commonly called **SARS**, **MERS**, and **COVID-19** respectively.

Common Cold

- Although the common cold is usually caused by rhinoviruses, in about **15% of cases** the cause is a coronavirus
- The human coronaviruses **HCoV-OC43**, **HCoV-HKU1**, **HCoV-229E**, and **HCoV-NL63** continually circulate in the human population in adults and children worldwide and produce the generally mild symptoms of the common cold
- The four mild coronaviruses have a **seasonal incidence** occurring in the **winter months** in temperate climates
- There is **no preponderance in any season** in tropical climates

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Stages of Coronavirus Infection

There are three general phases of infection with **SARS-CoV-2**, the coronavirus that causes COVID-19:

1. Incubation Period

- This is the time between getting infected and when symptoms appear

- In general, you may see symptoms start **two to 14 days** after infection
- The incubation period varies among individuals, and it varies depending on the variant
- Even though you do not have symptoms in the incubation period, you can transmit the coronavirus to another person during this stage
- If you suspect you were exposed to someone with COVID-19, you should self-quarantine, watch for symptoms and consider getting tested **four or five days** following the exposure

2. Acute COVID-19

- Once symptoms appear, you have entered the acute stage
- You may have fever, cough and other COVID-19 symptoms
- Active illness can last **one to two weeks** if you have mild or moderate coronavirus disease, but severe cases can last months
- Some people are **asymptomatic**, meaning they never have symptoms but do have COVID-19
- If you develop symptoms or suspect you are asymptomatically infected, call your health care provider, follow testing guidelines, and follow all isolation and safety guidelines

3. COVID-19 Recovery

- Post-COVID-19 symptoms, such as lingering cough, on and off fever, weakness, and changes to your senses of smell or taste, can persist for **weeks or even months** after you recover from acute illness
- Persistent symptoms are sometimes known as **long COVID-19**

Prevention and Treatment

Vaccines

- A number of vaccines using different methods have been developed against human coronavirus **SARS-CoV-2**
- Vaccines are available for animal coronaviruses although their effectiveness is limited
- In the case of outbreaks of highly contagious animal coronaviruses, such as **PEDV**, measures such as destruction of entire herds of pigs may be used to prevent transmission to other herds

Antiviral Targets

- Antiviral targets against human coronaviruses have also been identified such as:
  - **Viral proteases**
  - **Polymerases**
  - **Entry proteins**
- Drugs are in development which target these proteins and the different steps of viral replication

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Laboratory Diagnosis of Coronaviruses

Current Research Focus

In order to stop the spread, researchers worldwide are working around the clock aiming to develop reliable tools for early diagnosis of severe acute respiratory syndrome (SARS-CoV-2) understanding the infection path and mechanisms.

Diagnostic Methods

1. Nucleic Acid-Based Molecular Diagnosis

- **Real-time reverse transcription polymerase chain reaction (RT-PCR) test** is considered the **gold standard** for early diagnosis of SARS-CoV-2

2. Antibody-Based Serology Detection

- **Ineffective for the purpose of early diagnosis**
- A potential tool for serosurveys, providing people with immune certificates for clearance from COVID-19 infection

3. Comprehensive Diagnostic Methods

Methods used for diagnosis of the discovered human coronavirus (SARS, MERS, COVID-19) include:

- **Nucleic acid detection**
- **Gene sequencing**
- **Antibody detection**
- **Antigen detection**
- **Clinical diagnosis**

Test Result Interpretation

- Test results may remain positive for **weeks to several months** following infection, but this does not necessarily mean you are still infectious
- Most people are no longer infectious beyond the recommended isolation precautions period
- If the infected person has conditions that cause severe immunosuppression, contact your health care provider to determine how long he should be isolated and how to determine when he is no longer potentially infectious to others

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End of Lecture

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