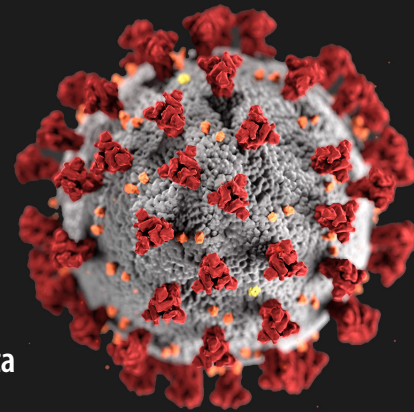


Pandemic Pandemonium: Why Can't We Just Treat COVID-19?

by

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Part I – The Need to Quarantine

“But I want to go out with my friends! This is *so* unfair!” Kat wailed from across the room while her mom and dad sat stone-faced on the couch. The sixteen-year-old high school student thought this sounded like torture.

“We’re sorry, sweetheart, but one of your mother’s employees has tested positive for COVID-19. Since they share an office, we have to stay here for 14 days to make sure we’re all okay,” Dad stated in a matter-of-fact voice.

“But that’s silly! We only spent one hour in mom’s office yesterday before soccer practice. We weren’t even there that long!” Megan, Kat’s twin sister, scoffed.

“Well, that’s all it takes,” Mom retorted. “We are going to listen to the recommendations of the doctors and that’s final. We are quarantining ourselves here for two weeks.”

Megan and Kat left the room and headed to their shared bedroom. Megan, the daughter who always needed evidence to back up any statement, immediately took out her laptop and started searching for answers. Kat watched over her shoulder.

Megan wanted to know all about this disease. She had never heard of COVID-19, much less thought about getting it. Megan found information on the CDC website about the disease COVID-19 and about the virus that causes it, SARS-CoV-2. Based on the statistics she was seeing, she couldn’t figure out why her mom was so worried. It looked as though this was a disease to be worried about if you were elderly, but she and her sister were sixteen, so she figured that they should be just fine.

(Use the following sources that Megan consulted to help you answer the questions below.)

- Centers for Disease Control and Prevention. Coronavirus (COVID-19).
<<https://www.cdc.gov/coronavirus/2019-nCoV/index.html>>
- World Health Organization. Q&A on coronaviruses (COVID-19).
<<https://www.who.int/news-room/q-a-detail/q-a-coronaviruses>>

Questions

1. What are the symptoms of COVID-19?
2. What are the mechanisms of transmission of SARS-CoV-2?
3. What is a quarantine? How long does a quarantine usually last? On what factors does the length of a quarantine depend? Why are Megan and Kat’s family in a 14-day quarantine?
4. Based on the information above, do you think Megan and Kat are at risk of developing COVID-19? Why or why not?

Part II – Exploring the Structure of SARS-CoV-2

Kat noticed that one of the recommendations from the CDC for prevention of COVID-19 was to “wash her hands with soap,” and she giggled outwardly. That was obvious! She had been washing her hands since she was a toddler before meals. She pulled out her own laptop and started looking for “real scientific” answers rather than what she thought was the somewhat obvious information Megan was finding.

Kat started researching SARS-CoV-2 and its structure. When looking at pictures of the coronavirus, Kat wasn't surprised to learn that the name meant “crown” virus. That made sense given that most of the pictures she saw looked like the virus had a halo or crown surrounding it. But what was the crown made of?

She quickly learned that SARS-CoV-2 belonged to a bigger family of viruses called the SARS-associated coronaviruses. She found out that like most viruses, it had a core containing nucleic acid and several associated proteins. She went on to read that unlike the other typical viruses she had learned about in school, the SARS-associated coronavirus has characteristics that make it slightly different. She discovered the following characteristics of the SARS-associated coronavirus virion, or virus particle:

- It is an RNA virus, meaning it has a nucleic acid center made of RNA and not DNA.
- It has a protein associated with the RNA called nucleocapsid protein.
- It has an outer phospholipid bilayer surrounding the structure that has several different types of glycoproteins embedded within it.
- The glycoproteins found in the viral membrane are spike, envelope and membrane glycoprotein.
- There are other accessory proteins used by the virus that help with infection and replication in host cells.

Kat found an illustration (Figure 1). “It has a phospholipid membrane,” she gasped, “That’s why I need to use soap and wash my hands to clean off this virus!” She thought about this for a moment and realized learning about lipids in her high school chemistry class was finally coming in handy. This was just the thing to destroy the outside of a coronavirus! Maybe Megan’s research hadn’t been so silly after all.

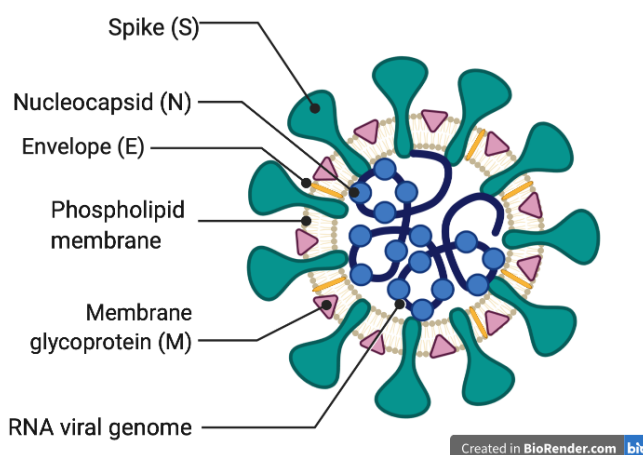


Figure 1. Schematic drawing of SARS-CoV-2.

Questions

Answer the following questions. If you use an outside source, be sure to include a citation.

1. What are the structural and functional differences between DNA and RNA?
2. List one human-infecting virus that has a DNA-based genome.
3. What is a glycoprotein? Where are they found in human cells? List some of their functions.
4. Hypothesize as to why coronaviruses may have glycoproteins in their membranes. What may be the purpose and function of these structures?
5. Describe the structure of a phospholipid and a phospholipid bilayer. Indicate the polar and nonpolar parts of the structure for each.
6. Describe how soap could chemically destroy a coronavirus virion.

Part III – How Does SARS-CoV-2 Infect Me?

Kat decided to find out more about the mechanism of infection of SARS-CoV-2 as compared to other viruses she had heard of like HIV and herpes. She knew many viruses have a lytic cycle. In the lytic cycle, viruses actively replicate themselves inside the host utilizing the host machinery, and eventually destroy the host cell.

Coronaviruses, she found, are viruses that seemed to be something unlike the typical viruses she had studied. She considered the steps of coronavirus infection below:

Step 1: SARS-CoV-2 is recognized by and attaches to the host cell via the spike glycoproteins in the viral membrane of the virus.

Step 2: SARS-CoV-2 is engulfed by the host cell.

Step 3: The original infecting SARS-CoV-2 RNA is released, but remains in the host cytoplasm.

Step 4: A specific section of the original infecting SARS-CoV-2 RNA is translated to make RNA-dependent RNA polymerase.

Step 5: The viral RNA-dependent RNA polymerase simultaneously makes complete copies of the genomic RNA to be packaged into new virions and transcribes specific sections to mRNA as templates for translation from the original infecting RNA.

Step 6: The newly synthesized coronavirus viral mRNA is translated into viral proteins like viral proteases, structural proteins, and RNA-dependent RNA polymerase using host ribosomes.

Step 7: Many of the newly synthesized viral proteins are processed for packaging into new virions.

Step 8: Partially complete virions are assembled and then bud from the host taking with them host membrane.

Questions

1. Describe the steps of lytic infection typical to a DNA virus like herpes simplex virus.
2. How are the steps of SARS-CoV-2 infection different from lytic infection of a DNA virus? How are they similar?
3. How might an RNA-based genome result in an increased infection rate? What are some potential complications to this infection strategy?
4. What is the central dogma of biology? How does coronavirus defy traditional models of central dogma?
5. Fill in the table below comparing four different viruses. Use resources found at either/both of the following websites to guide you in the process:
 - Centers for Disease Control and Prevention. <<https://www.cdc.gov>>
 - National Center for Biotechnology Information. <<https://www.ncbi.nlm.nih.gov>>

Table 1. Comparison of four different viruses.

<i>Name of Virus</i>	<i>SARS-CoV-2</i>	<i>Herpes Simplex Virus (Type-1)</i>	<i>HIV</i>	<i>Influenza B</i>
<i>Symptoms</i>				
<i>Incubation period (time of acquisition to onset)</i>				
<i>Type of cell the virus infects</i>				
<i>Nucleic acid type</i>				
<i>Accessory proteins</i>				
<i>Does the virion have a membrane? (Yes/No)</i>				
<i>Does virus integrate into the host genome? (Yes/No)</i>				
<i>Treatment</i>				

Part IV – The Unfortunate Diagnosis

After almost a week of being home under quarantine, the girls started to get restless. They went out to play soccer in the backyard, quickly passing the ball back and forth in a warm-up drill. Kat began to make mistakes that she usually didn't make and just seemed "out of it" to Megan.

"One week off from practice and you can't even play anymore?" Megan quipped with a huge grin on her face. "I guess, I'm now the better player."

"No. I don't feel very good," Kat said looking at the ground. "I'm just so tired and it's like I can't get enough air. I'm going inside."

That afternoon, Kat began running a fever. Her symptoms became increasingly worse to the point where her parents simply couldn't keep her fever in check. The girls' parents took Kat to the emergency room the next day to find out that she was positive for COVID-19. While in the hospital and receiving expert medical care, Kat's breathing became more and more labored. The doctors even began discussing the possible need of a ventilator to help her breathe.

Pleading with the doctors for some kind of help, Kat's parents became desperate.

"Isn't there something you can do to help treat this virus in her? Can't you give her penicillin? Give her that!" Kat's dad began yelling frantically.

"I'm sorry, but that just won't work against this virus. Antibiotics, like penicillin, only work on bacteria. Antivirals are the pharmacological agents that we usually use to treat viral infections. I'm afraid that we don't have any available to use against COVID-19. There is nothing we can do right now other than help her rest and keep her comfortable. She will likely be okay if we give her time to recover."

Kat's mom simply wouldn't give up hope. She asked nurses and hospital staff what kind of antivirals were available. She found the following list:

- Oseltamivir is an antiviral that treats influenza. It is a neuraminidase inhibitor.
- Acyclovir is an antiviral used to treat herpes simplex virus (HSV). This drug stops replication of viral DNA.
- Raltegravir is an antiviral used to treat HIV. This drug stops integration of HIV into the host genome.
- Lamivudine is an antiviral used to treat HIV. This drug stops the action of the enzyme reverse transcriptase. Reverse transcriptase is the enzyme that copies HIV RNA into DNA.
- Maraviroc is an antiviral used to treat HIV. It blocks entry of the virus into macrophages and T-Cells.

It didn't appear that any one of these would work for Kat. Kat's mom began crying. She sat in the waiting room chair in disbelief. How had she missed the signs and let this happen?

Questions

1. What is an antibiotic? Why won't an antibiotic be effective in treating COVID-19?
2. What is an antiviral? When are antiviral treatments most effective? How do antivirals avoid harming the host?
3. For each of the antivirals Kat's mom identified, suggest a reason why they will not work for SARS-CoV-2.
4. Using what you have learned about COVID-19, suggest a possible target or target step in the SARS-CoV-2 life cycle for an antiviral drug target. Consider how your proposed antiviral target or target step may impact the health or well-being of the human host.

Part V – What Do We Do Next?

At home, Megan struggled with the news that Kat was going to stay in the hospital for some time. She decided she wanted to write an email to their soccer team telling them of Kat's diagnosis. She thought it was her job to tell them that they were at risk, and they shouldn't take COVID-19 as lightly as she and her sister had.

In time, Kat recovered, but Megan and her dad never developed outward symptoms of COVID-19. The girls' mom developed a mild case of the disease with a slight cough and fever, but never anything like what Kat had. Later tests showed everyone in the family had been exposed to the disease, but only Kat developed a severe symptomatic case. Megan and her parents had been lucky.

Assignment

Adopting the role of Megan, draft an email to Kat's teammates. Consider the following when drafting your email:

- What and how much should you tell the team about the situation with your sister?
- Is it ethical to share the specifics of her situation?
- How much advice (if any) would you provide to the team about quarantine and what to do next?
- Do you think quarantines are effective? Why or why not?
- How would you make the team believe that your advice is real and not anecdotal?
- Would you share any of the science you had learned?
- What will be your next steps going forward?



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