Viruses and Vaccines

CONTENT PRIMER

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Viruses were first detected within tobacco plants infected with tobacco mosaic disease. A Russian botanist, Dmitri Ivanovsky, provided the first evidence for viruses when he showed that extracts from infected tobacco plants could still infect healthy plants even after the extracts had been run through an extremely fine filter to remove all bacteria. However, scientists were unable to clarify whether they had detected an extremely small form of bacteria or some other new infectious agent. Little was known about viruses for some time after their initial discovery until the widespread use of the electron microscope when scientists gained the capability to detect viruses more directly.

Viruses are unique, non-cellular structures and therefore lack many of the characteristics of cellular organisms, such as having membrane-bound organelles, ribosomes, cellular membranes, etc. They are, overall, very simple and have only two or three components. Viruses have a nucleic acid genome that is either RNA or DNA, either single- or double-stranded. The nucleic acid is covered by a protein coat called a capsid. Some viruses have an additional membrane called an envelope that covers the capsid (Fig. 1). Viruses must have a living host cell to survive and replicate. Once a virus infects a host, it uses the host's cellular machinery to copy the viral genome and assemble new viral capsids. Eventually, the host cell is triggered to release the new viruses, sometimes destroying the host cell in the process.

Viruses are sometimes classified by the shape of their capsid, but it provides relatively little information about what type of organisms the virus is capable of infecting. The combination of differences in viral genome and the structure of their capsid and envelope create a variety of viruses capable of infecting a variety of hosts.

Types of Virus Shapes

- Filamentous: the long, thin, worm-like shaped.
- Isometric or icosahedral: spherical-shaped viruses.
- Enveloped: viruses that have membranes that surround their capsids.
- Complex / Head and tail: these viruses infect bacteria, they have a head that is similar to icosahedral viruses, and a helical-shaped tail.

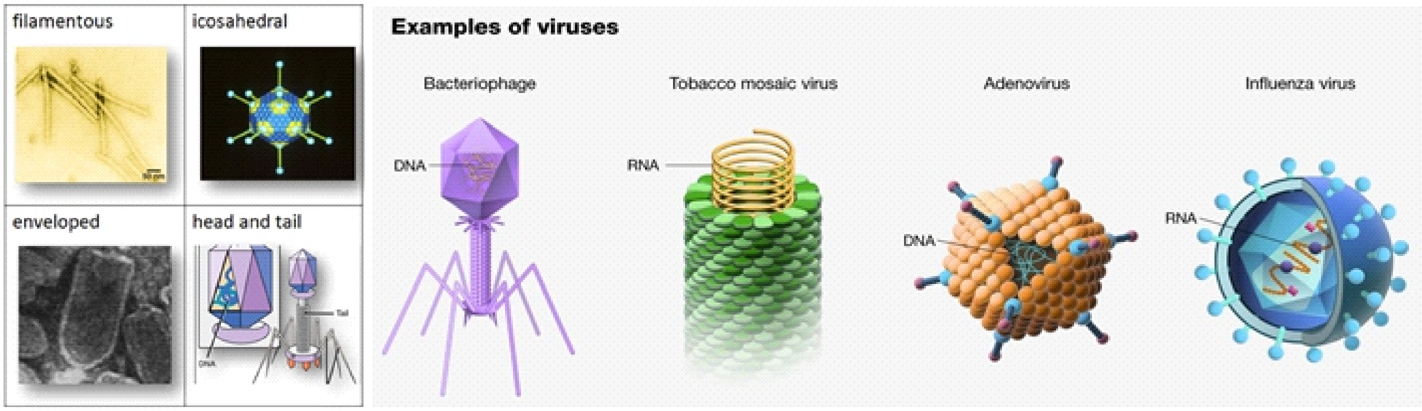

Figure 1. *Shapes and examples of viruses (image from NIH)*

Viruses can have either DNA or RNA as their nucleic acid. DNA viruses generally need to replicate within the nucleus of the host cell and the DNA is often double-stranded (but can be single-stranded). A few DNA viruses do have their own polymerases for DNA replication which means they can replicate in the cytoplasm of the host cell. RNA viruses can replicate in the cytoplasm and are more often single-stranded (but can also be double-stranded). Because RNA is less stable than DNA, especially when single-stranded, and RNA polymerase lacks the proof-reading and correction abilities that DNA polymerase has, RNA viruses very prone to mutation. SARS-CoV-2 and influenza are both examples of RNA viruses with many new and continually evolving strains due to mutations. Smallpox is an example of a DNA virus which is much more stable over time.

How do Viruses Infect?
Generally, there are four steps of infection.

Step 1: Attachment: The virus attaches itself to the target cell.
Step 2: Penetration: The virus is brought into the target cell.
Step 3: Replication and Assembly: The viral DNA or RNA is replicated, and viral proteins are assembled. If it is an enveloped virus, then it loses its envelope before the genome is replicated.
Step 4: Egress (Release): New viral particles are released.

How do Vaccines Work?
Because viruses are so simple, they can be challenging to target with drugs. Antibiotics often work by disrupting essential functions or structures in bacteria such as the cell wall that protects them, but viruses lack these structures and cellular machinery, rendering antibiotics useless against the viruses themselves. Vaccines remain the primary form of protection against viral infection. Generally, vaccinations work as a preventative measure building immunity prior to an unintended infection The goal of vaccination is to boost the host's immune system prior to catastrophic infection. Some vaccines can also work during the very early stages of an active infection. The rabies vaccine, for example, with early enough application, can prevent viral particles from entering nervous tissue resulting in fatal neurological damage. Similar research is underway regarding the Ebola virus.

Vaccines utilize “live” viruses, killed viruses, or sub-particles of viruses. “Live” viruses, which are typically the most effective form of vaccination, utilize a weakened (attenuated) virus for preexposure. Some vaccines do not require many alterations as the mutation rate of the virus they protect against is very low and the viruses are still very similar to their original form. However, for viruses such as the influenza virus and HIV, the mutation rate is quite rapid, meaning that new forms of the vaccine are required to combat new, unique strains. Influenza mutates so rapidly that a new vaccine is developed every year. Scientists determine what strains are likely to be the most prevalent in the upcoming flu season and develop the vaccine against those strains, which is why there is a new flu vaccine every year and some years it is a better “match” than others. HIV is a uniquely complicated virus to treat because its rate of mutation is so high, which is one reason a vaccine has been challenging to develop. Instead, current treatment of HIV often involves multiple drugs to block the rates of HIV virus replication. The antivirals, which are drugs that target the mechanisms used by viruses during replication, help keep the viral load lower, protecting both the infected individual and others.

References
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