Antivirals

Viruses

"A large group of infectious agents ranging from 10 to 250 nm in diameter, composed of a protein sheath surrounding a nucleic acid core and capable of infecting all animals, plants, and bacteria; characterized by total dependence on living cells for reproduction and by lack of independent metabolism".

- "Dictionary of Bioscience", McGraw-Hill (1997)

Unlike bacteria, viruses have no nucleus or cytoplasm and so they are NOT cells. They do not feed or grow or excrete and they can only reproduce inside cells of host living organisms. The virus injects its DNA (or RNA) into the cytoplasm of the host cell and then "takes over", causing the host cell to die or become altered. This causes the symptoms of the viral infection. The host cell produces new DNA (or RNA) and forms many new viruses, which are released to infect other cells.

There are many types, shapes and structures of virus but they all have:

1. Central core of DNA or RNA
2. Coat ("capsid") of regularly packed proteins ("capsomeres")

Common viral infections include: colds, influenza, chicken pox, and herpes.

How Antivirals Work? (B.7.3)

The body's own defense mechanisms are usually enough to overcome infections such as those mentioned above. Drugs are given to relieve symptoms (e.g. pain, fever). By the time these symptoms appear, the virus will be so numerous that antivirals will have little effect.

Recently, drugs have been developed to fight specific viruses. Some of the drugs work by altering the DNA/RNA of the host cell so that the virus cannot use it to multiply. **Acyclovir** works in this way to help fight the herpes virus that causes cold sores. Its structure is similar to deoxyguanosine (one of the building blocks of DNA) and the virus is "fooled" into using it as a building block and so multiplication is stopped.

Other drugs work by blocking enzyme activity within the cell. One example is **amantadine**, which is active against influenza. Influenza viruses use an enzyme called

neuraminidase to help them stick to the cell wall as they leave it. Amantadine inhibits the active site on the enzyme and so prevents the virus from leaving the cell.

One of the biggest problems with developing antivirals is that the viruses themselves regularly mutate, making the drug ineffective. This is especially true of the HIV virus.

AIDS (B.7.3)

AIDS (Acquired Immune Deficiency Syndrome) is caused by a **retrovirus** (contains RNA rather than DNA). The virus invades cells like white blood cells ("T-cells"), which normally activate the body's immune system. The body is then unable to fight infection.

When the virus enters a healthy cell, it uses an enzyme called **reverse transcriptase** to make virus DNA from its RNA template. It has proved very difficult to develop antivirals or a vaccine for HIV because of rapid mutation of the virus and because the health of the host cell is closely linked to the health of the virus. One drug that has had some success is AZT (zidovudine), which combines with the reverse transcriptase to build DNA and block the active site of the enzyme. The drug is therefore known as a **reverse transcriptase inhibitor**. AZT does not affect normal cells because only retroviruses use reverse transcriptase.

Other strategies that are being employed to tackle AIDS include:

1. The virus binds to a receptor on the host cell so: try to **alter the receptor site to prevent the virus from binding**.
2. The virus enters through the cell wall so: try to **alter the cell wall**.
3. Virus must lose its protective coat to release RNA so: try to **develop a drug that prevents the virus from losing its protective coat**.
4. The host cell produces new viral RNA and protein so: try to **alter the genetic material of the virus to inhibit production of RNA/protein**.
5. New viruses are formed, which leave the cell and spread the infection so: **try to prevent the new viruses from leaving** (like amantadine for influenza).