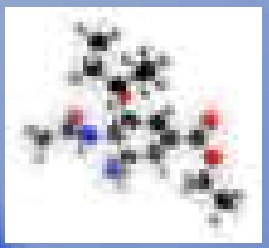


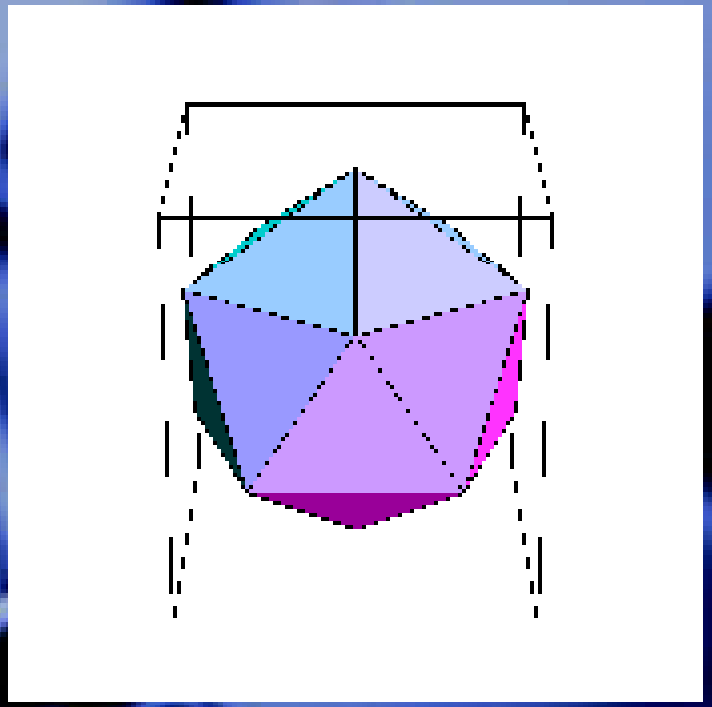
Antiviral Drugs: An Overview

The Outline

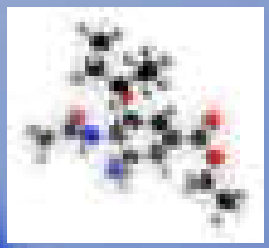
1. Viruses, what are they, who are they?
2. Virus Classifications
3. The virus, its hidden personal life
4. Methods of Attack
5. Building the Weapon: Drug Development
6. The Weapon of Choice: Antiviral Drugs
7. Conclusions and Overview

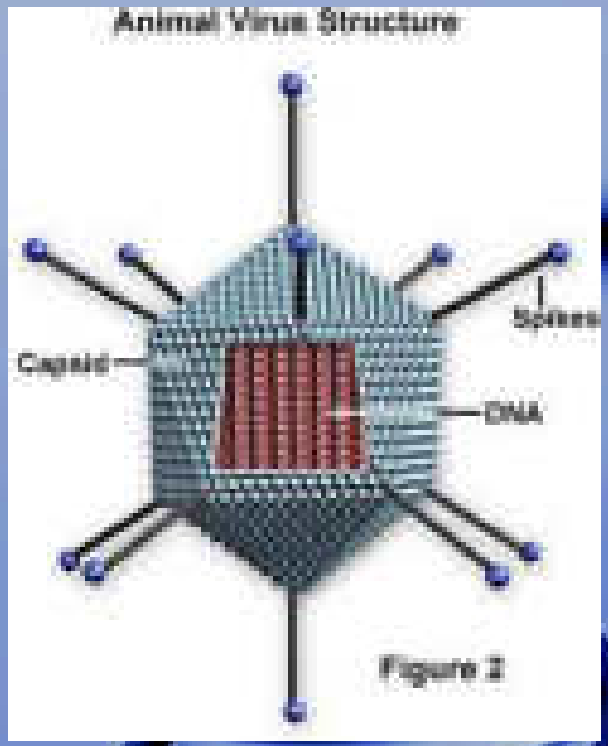
Viruses, what are they?

- Viruses do not fit the mold for a living organism
- Viruses are all parasites of the living
- They cannot make anything on their own, they use the cell's materials to build themselves
- Origin: Speculated to be rogue segments of DNA that have taken a parasitic role



Viruses, who are they?





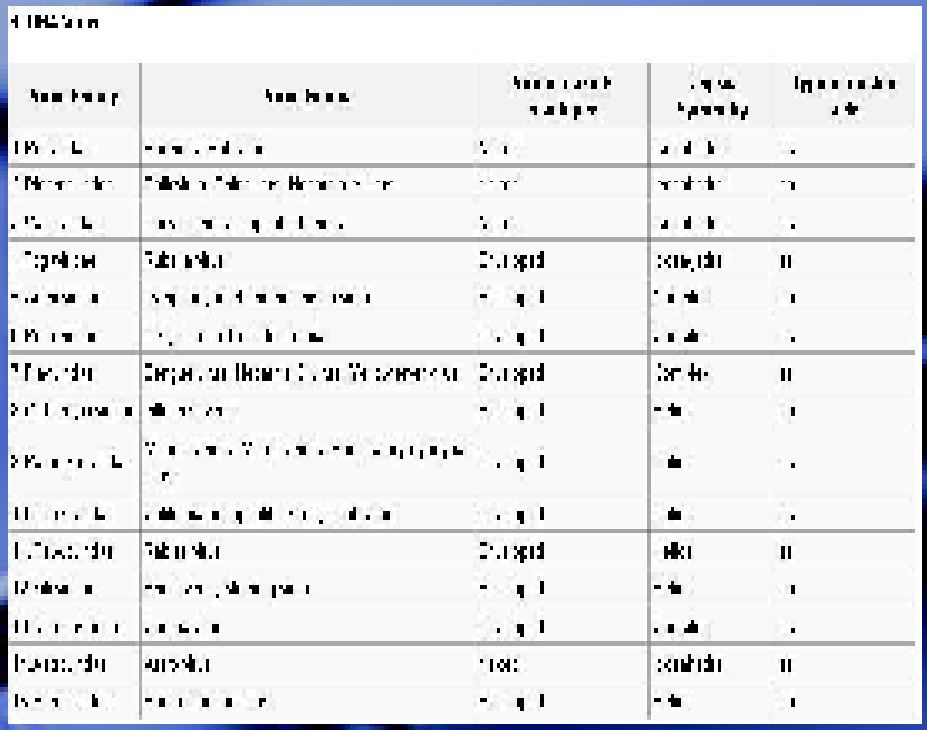
- The Capsid: A protein shell of capsomer subunits. It has three purposes: to Shield, Attach, and Penetrate
- The Envelope: Hybrid combination of cell lipids and virus proteins, permits attachment (note spikes)
- Nucleic Acids: Either DNA or RNA enclosed within the capsid that is later used to replicate more viruses within the host cell

Virus Classifications

- Two types of Classification, The Baltimore System and the International Committee on Taxonomy of Viruses (ICTV)
- The ICTV Version uses a common biology taxonomy approach and is the current accepted standard of the 80 families and 4000 species of Virus
- The Baltimore System was devised by Nobel prize winning biologist David Baltimore and separates viruses according to nucleic acid type (DNA or RNA), method of replication (positive-sense, negative-sense) and the number of strands (single or double strand)

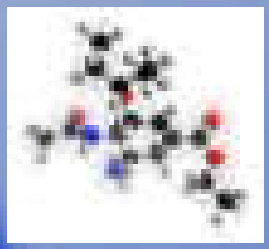
Virus Classifications

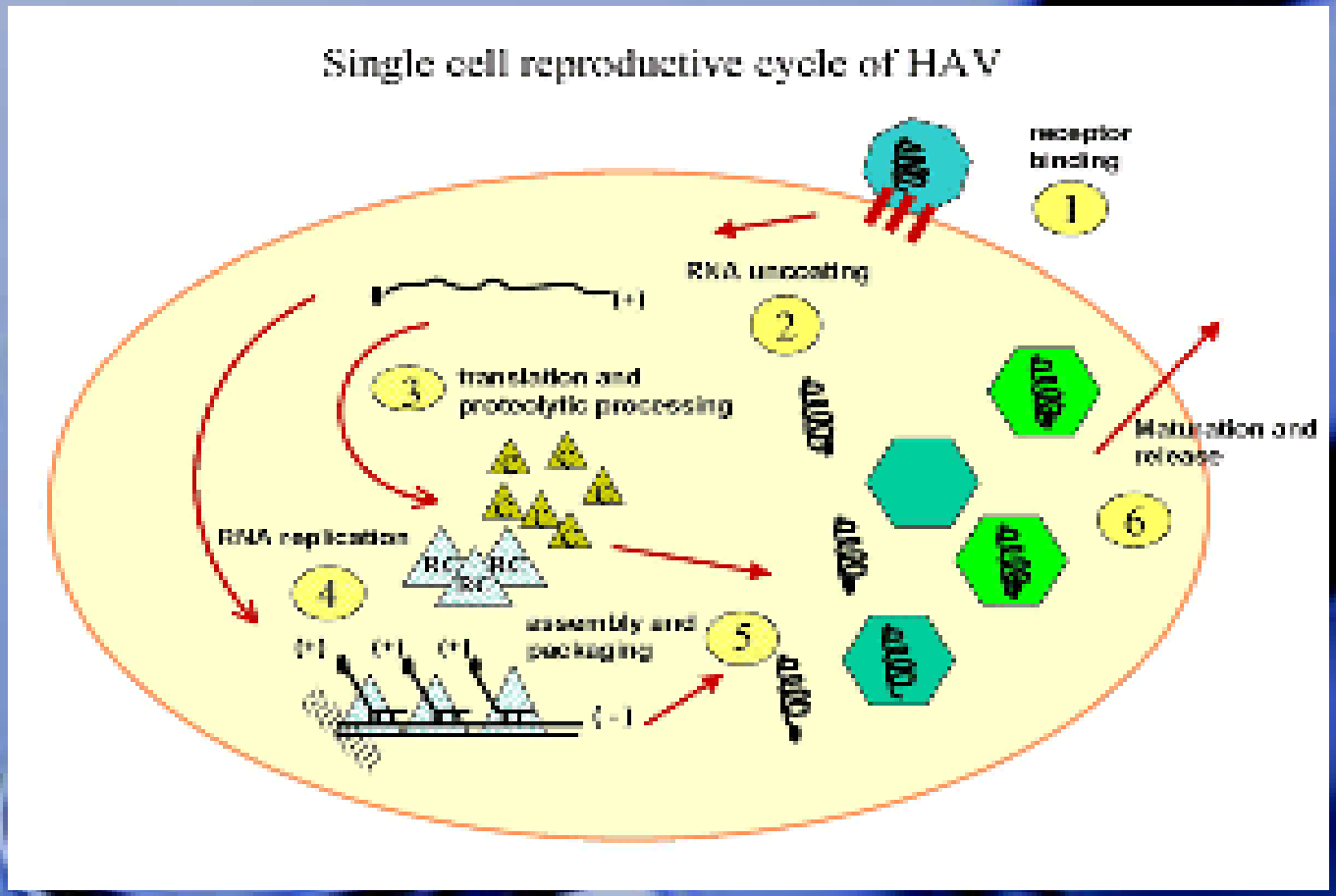
- Many Families are not classified in the system due to grouping difficulty



- Some RNA Viruses are positive-sense or negative sense, in other words they can directly act like mRNA (+) or they need a RNA transcriptase to be included in the virus (-)

The Virus' Personal Life

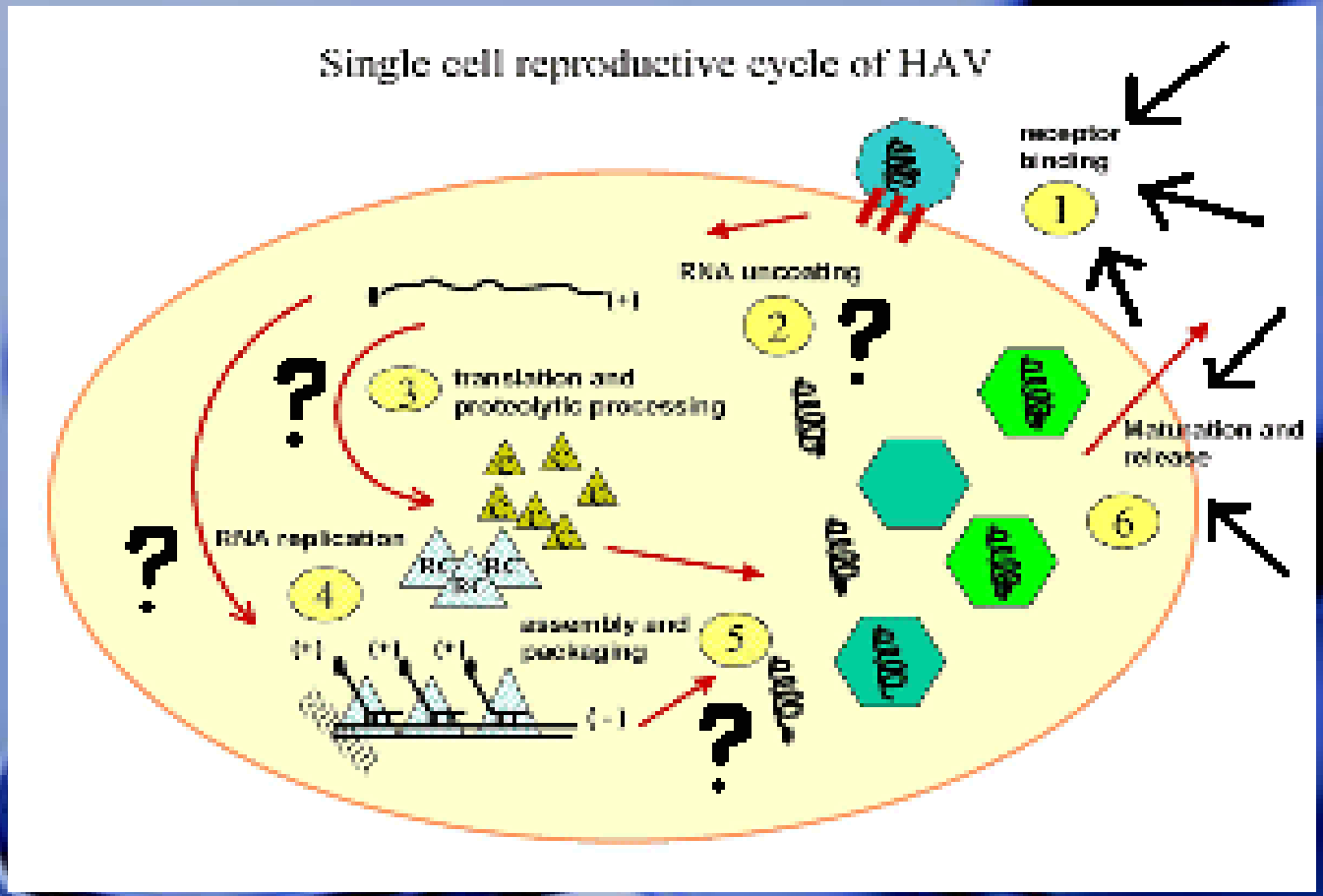




Antivirals, why?

- Vaccines are effective at prevention but what about the patient that is already infected?
- Viruses can be very swift and deadly and a quick method of curing a patient is needed
- The market is huge and a remedy would bring about solutions to viral infections such as: Influenza, HIV, Herpes, Hepatitis B, Smallpox, Ebola, Rabies, etc.

Methods of Attack



Methods of Attack

- Viruses still need more study to understand their structure and life cycle
- The most effective methods so far can only attack by preventing the virus from attaching to the cell and from leaving the cell

Drug Development

- Viruses are now becoming better understood and several viral genomes have been properly mapped. Scientists are now looking for the best drug targets
- The main point of interest is any viral protein that the host organism does not normally produce
- Once these viral proteins are identified they are tested using a large scale screening process to test for effectiveness

Drug Development

- Antiviral candidates are tested in mass quantities
- Antiviral drugs generally have strange side effects and a high toxicity
- As with any pathogenic drug, Viruses evolve and develop immunity. Thus the need for new drugs always exists

Drug Development

There are several known methods that the makers of Antiviral drugs are looking at, including:

- Prevention of Viral Entry
- Targeting the RNA/DNA replication in the cell
- Targeting the transcriptase factors for Viral DNA
- Destroying Viral proteases so that viral proteins are not cut and rearranged in optimal order
- Stopping the release of the mature viruses from the host cell

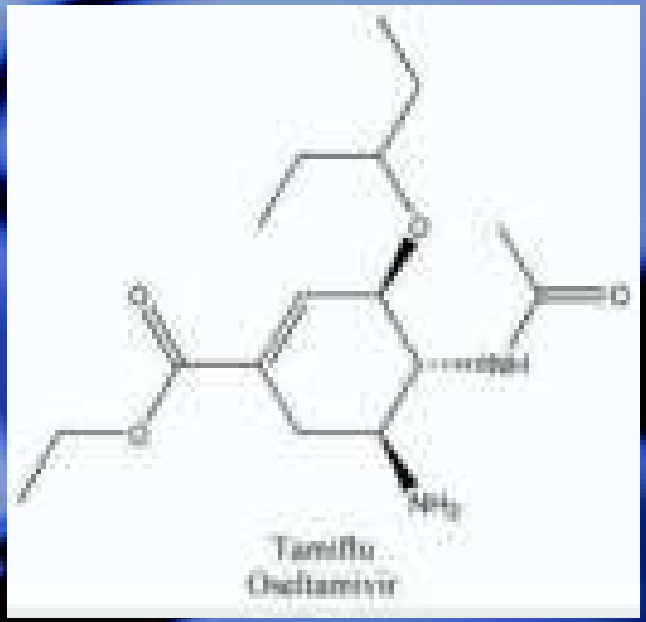
The Weapon of Choice: Antiviral Drugs

Anti-herpesvirus	Aciclovir, Cidofovir, Docosanol, Famciclovir, Fomivirsen, Foscarnet, Ganciclovir, Idoxuridine, Penciclovir, Trifluridine, Tromantadine, Valaciclovir, Valganciclovir, Vidarabine
Anti-influenza agents	Amantadine, Arbidol, Oseltamivir, Peramivir, Rimantadine, Zanamivir
Antiretroviral: NRTIs	Abacavir, Didanosine, Emtricitabine, Lamivudine, Stavudine, Zalcitabine, Zidovudine
Antiretroviral: NNRTIs	Tenofovir
Antiretroviral: NNRTIs	Efavirenz, Delavirdine, Nevirapine, Loviride
Antiretroviral: PIs	Amprenavir, Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir, Nelfinavir, Ritonavir, Saquinavir, Tipranavir
Antiretroviral: Fusion inhibitors	Enfuvirtide
Other antiviral agents	Adefovir, Fomivirsen, Imiquimod, Inosine, Interferon, Podophyllotoxin, Ribavirin, Viramidine

Drug Examples

Tamiflu-

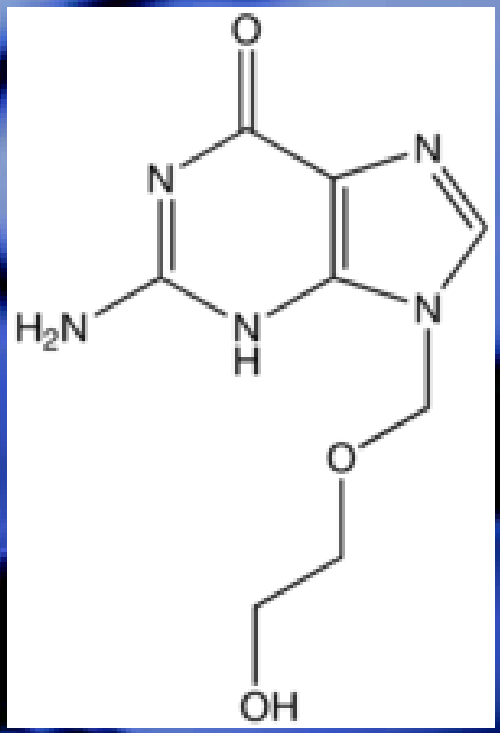
- Recently sold to 40 countries to battle avian flu
- Prevents the mature viruses from leaving the cell
- It is a neuraminidase inhibitor, it works on both influenza A and B
- Neuraminidase is an enzyme found on the virus which cleaves sialic acid from cell membrane, leading to a more effective release of viruses. mechanism



Drug Examples

Aciclovir-

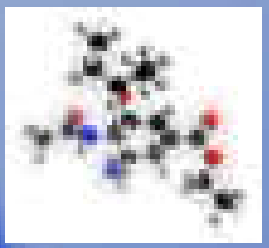
- A widely used antiviral with main implications in the treatment of herpes
- Seen as a “new age” in antiviral therapy, Gertrude Elion, its creator, was given the Nobel prize for medicine in 1988
- It is a nucleoside analogue and prevents viral replication in infected cells



Conclusions: Viruses of the future?

- With further understanding of Virus Genomes and virus' receptors, antiviral drugs will be more effective
- An understanding of the processes within the cell might lead to whole new classes of antiviral drugs
- Antiviral drugs are very experimental as of right now and hopefully with further discoveries, new processes of synthesis will be discovered

What just happened?



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