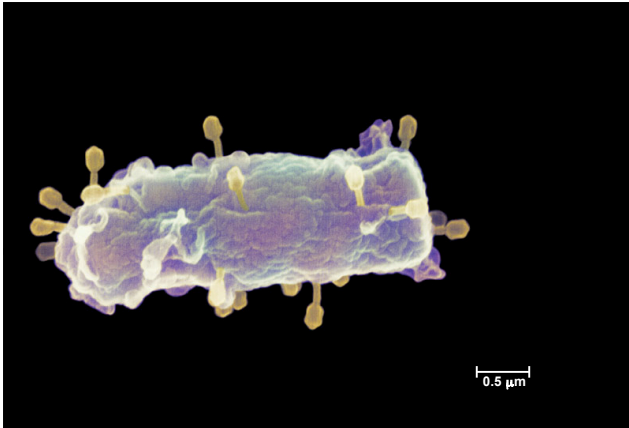


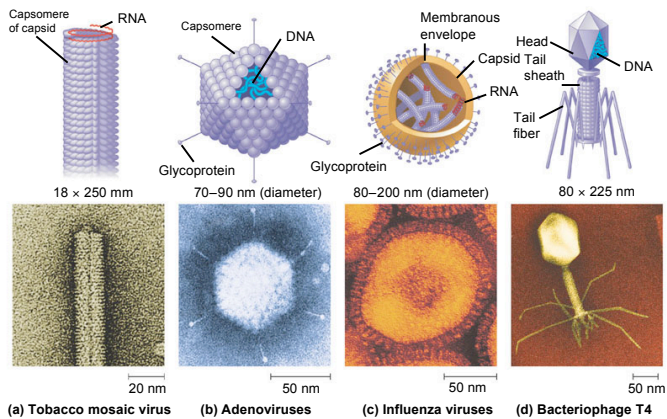
Lecture 29: Viruses



Lecture outline 11/11/05

- Types of viruses
 - Bacteriophage
 - Lytic and lysogenic life cycles
 - DNA viruses
 - Influenza
 - HIV
 - RNA viruses
- Prions
 - Mad cow disease

Figure 18.4 Viral structure



Viral reproductive cycle

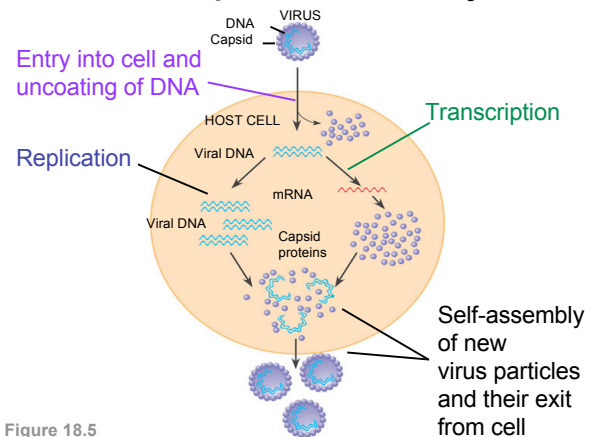


Figure 18.5

A **capsid** is the protein shell that encloses the viral genome

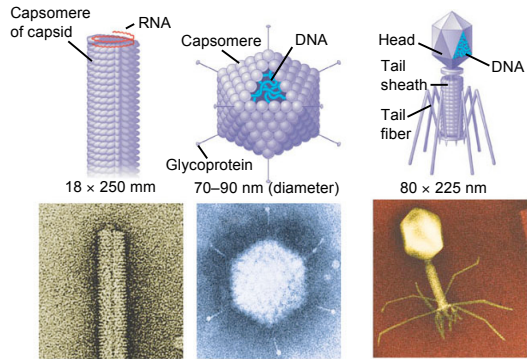


Figure 18.4a, b (a) Tobacco mosaic virus (b) Adenovirus (d) Bacteriophage T4

Viral Envelopes are derived from the membrane of the host cell

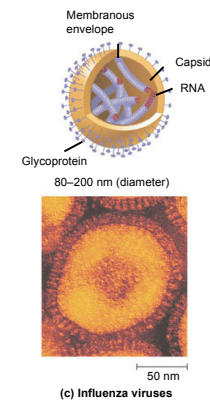


Figure 18.4c

Bacteriophage

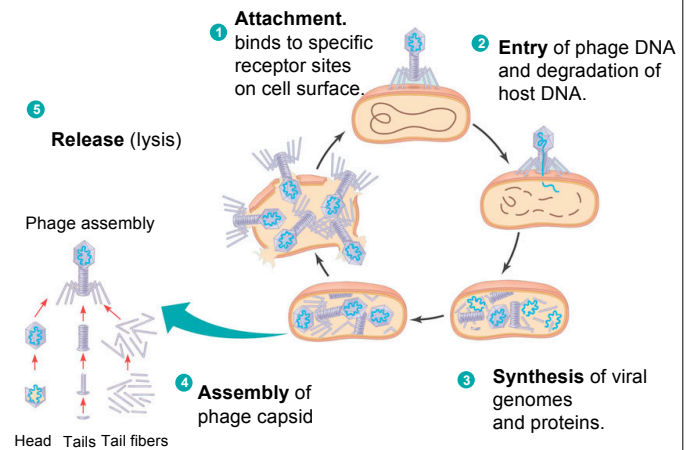
- Viruses of bacteria have been studied for decades

- T1, T2, T4
 - "virulent"
- Lambda
 - "temperate"

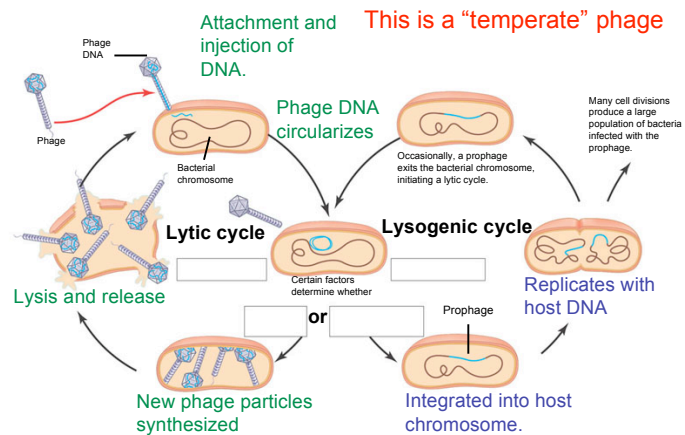


[See the animation](#)

The lytic cycle of T4



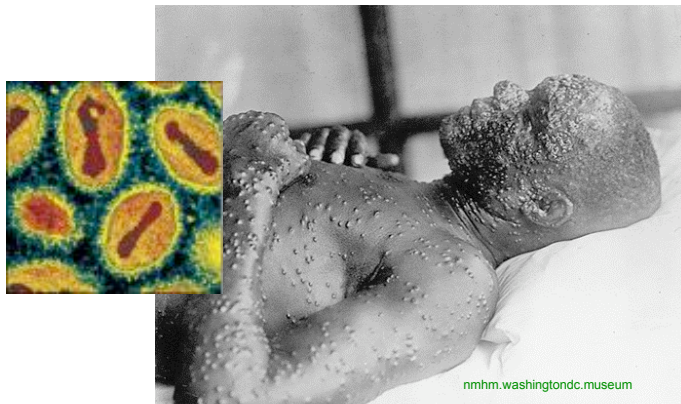
The lytic and lysogenic cycles of phage λ



Classes of Animal Viruses

	Genome Type	Viral coat	Examples
DNA Viruses	ds DNA	No	Herpes, chickenpox
	ss DNA	Yes	Smallpox
RNA Viruses	dsRNA	no	Tick fever
	ss RNA (serves as mRNA)	no	Rhinovirus SARS
	ssRNA (template)	yes	Influenza Ebola
	ssRNA (retrovirus)	yes	HIV

Smallpox

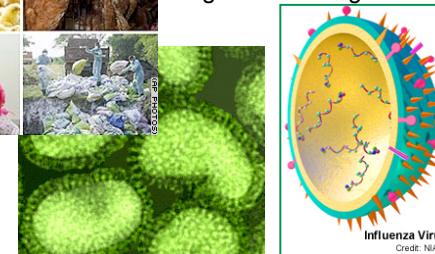


Influenza

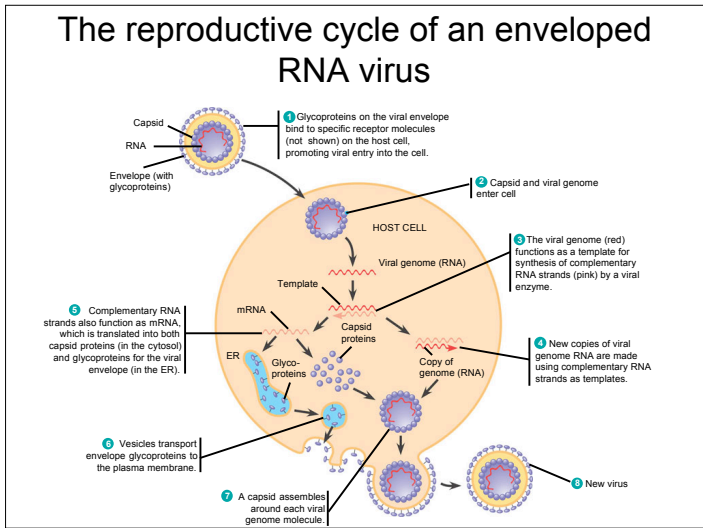


"H5N1"

One of the few viruses with genome in segments (8)



Spikes of hemagglutinin
And neuraminidase



Why are flu vaccines so hard to make?

- Flu strains are highly variable
 - Recombination among the viral gene segments
 - RNA polymerase has high mutation rate
- Now have some antiviral drugs (e.g. Tamiflu)
 - blocks the neuramidase enzyme so virus isn't released from cell

Influenza Virus
Credit: NAID

The New York Times
nytimes.com

October 6, 2005

Experts Unlock Clues to Spread of 1918 Flu Virus

By GINA KOLATA

The 1918 influenza virus, the cause of one of history's most deadly epidemics, has been reconstructed and found to be a bird flu that jumped directly to humans, two teams of federal and university scientists announced yesterday.

It was the culmination of work that began a decade ago and involved fishing tiny fragments of the 1918 virus from snippets of lung tissue from two soldiers and an Alaskan woman who died in the 1918 pandemic. The soldiers' tissue had been saved in an Army pathology warehouse, and the woman had been buried in permanently frozen

NEWS This Week
PAGE 32 Tagging along with sharks
34 & 35 2005 Nobelists in medicine, physics

Resurrected Influenza Virus Yields Secrets of Deadly 1918 Pandemic

VIROLOGY

As worries about a new flu pandemic mount, researchers have figured out the traits that made the 1918 influenza virus, which killed between 20 million and 50 million people, so virulent. Although a study on page 77 sheds new light on these questions, it raises a host of others because the researchers reconstructed the complete virus, which no longer existed anywhere on Earth.

The team resurrected the 1918 pandemic virus by using gene sequences fished from preserved tissue from a 1918 victim. The virus is as lethal as expected, killing mice more quickly than any other human flu virus known. Reconstructing the 1918 strain "had to be done, and it's produced some extremely interesting results," comments the researcher Robert Webster of St. Jude Children's Research Hospital in Memphis, Tennessee.

Although a scientific triumph, the experiment has stirred debate over safety procedures for handling such a deadly virus. Moreover, a new federal biosecurity board gave

"This work has to be seen in a positive light," says lead author Terrence Tumpey of CDC.

The research grows out of AFIP pathologist Jeffrey Taubenberger's efforts, begun in 1995, to sequence the genome of the 1918 flu virus. Working mainly with tissue from a victim found in permafrost in Alaska, he and others have been piecing together the virus's eight genes and characterizing their protein products.

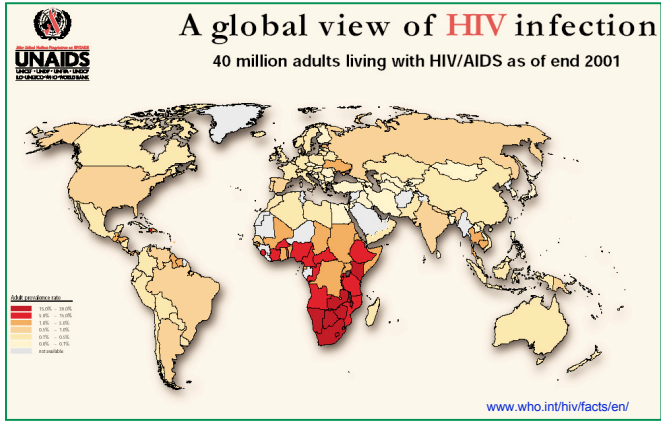
Last year, this work revealed the structure of the 1918 hemagglutinin (HA), the crucial protein that allows the virus to attach to and enter host cells.

They shipped these inert plasmids to Tumpey at CDC, who inserted them into cells to make live virus.

In this issue of *Science*, Tumpey, Taubenberger, and collaborators report how the reconstructed 1918 virus behaves. In experiments at CDC, the virus killed mice in 3 to 5 days and caused severe lung inflammation reminiscent of that reported by doctors who examined 1918 flu victims. The team also studied viruses with various combinations of 1918 genes and regular flu genes, which showed that "without that HA, the virus was not virulent," says Tumpey.

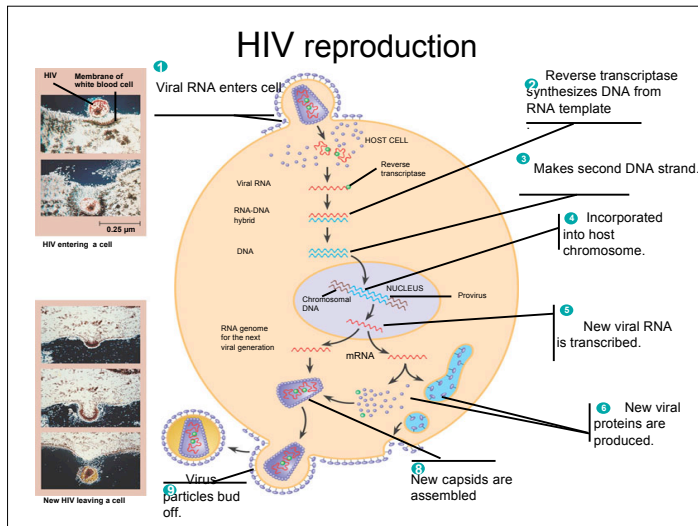
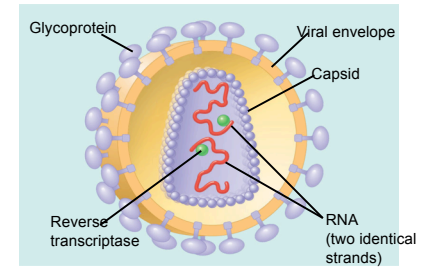
The 1918 flu had a couple of other tricks up its sleeve as well. One is that the virus doesn't need to rely on its host cells for the protease trypsin to cleave and activate the HA protein; instead, another surface protein, neuraminidase (NA), appears to help cleave the HA. That suggests the 1918 virus, like some highly virulent bird flu strains, can grow in any cell type, not just trypsin-laden lung cells. In addition, the 1918 flu's polymerase genes appear to allow it to replicate very efficiently in human

HIV

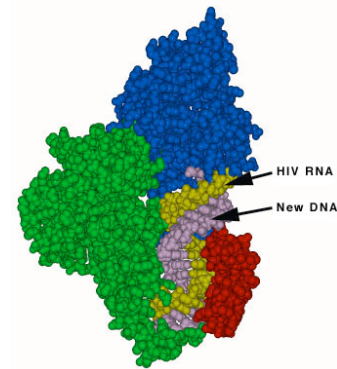


The structure of HIV, the retrovirus that causes AIDS

Only 9 genes in HIV:
Viral coat proteins
Reverse transcriptase
Integrase
Protease

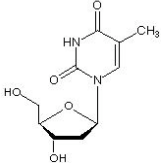


Reverse transcriptase is a special DNA polymerase

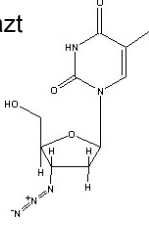


1. Copies DNA from an RNA template
2. Removes RNA template

thymidine



azt

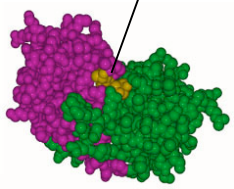


AZT

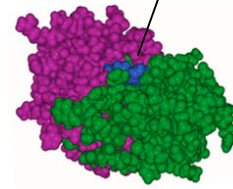
- Azidothymidine
 - a modified thymidine
- The first anti-retroviral drug
- Stops DNA synthesis because it does not have a 3'OH
- Originally developed as an anti cancer drug, but too many side effects

Protease inhibitors- another class of drugs for HIV

Protein in active site



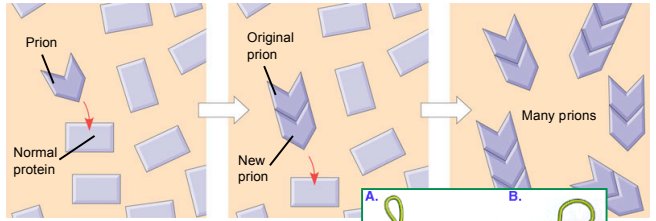
Inhibitor in active site



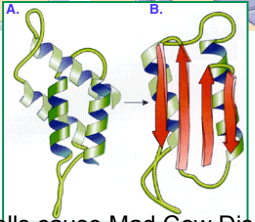
HIV initially produces one long polypeptide.
Protease is necessary to cut the polypeptide into individual enzymes

www.chemistry.wustl.edu/~edudev/LabTutorials/HIV/

Prions are infectious mis-folded proteins



Starts a slow chain reaction, causing regular proteins to assume the new shape



Altered PRP proteins in nerve cells cause Mad Cow Disease