HIV Infection and Epidemiology: Can There Be a Cure?

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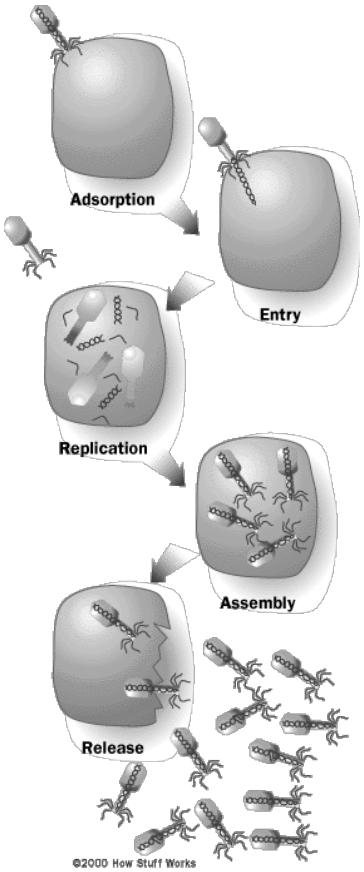
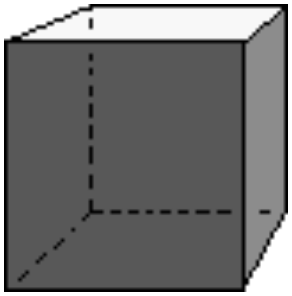
The Viral Life Cycle



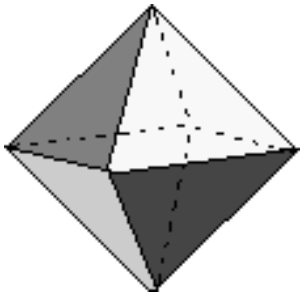
- A typical virus (DNA or RNA + protein) enters the host cell, makes more of itself, and exits.
- There are two major types of viruses: bacteriophage (left) infect prokaryotes, and other virions infect eukaryotes (animal or plant cells).

The Platonic Solids and Viruses

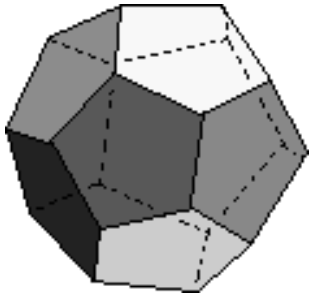
Tetrahedron



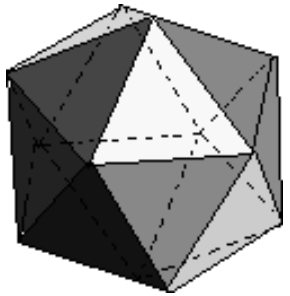
Cube



Octahedron



Dodecahedron

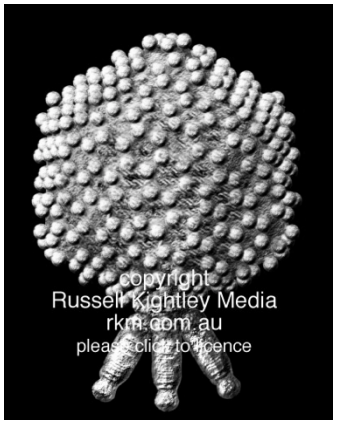


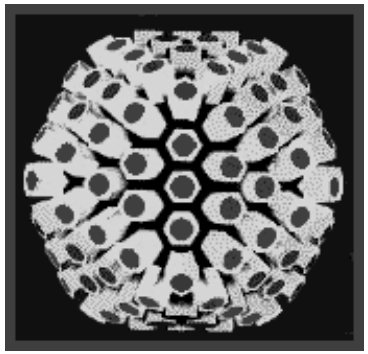
Icosahedron

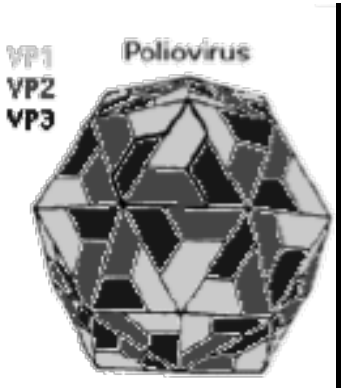
- Plato said that each of these 5 solids represented an "element" on earth: Tetrahedron for Fire, Cube for Earth, Octahedron for Air, Dodecahedron for the Cosmos, Icosahedron for Water.

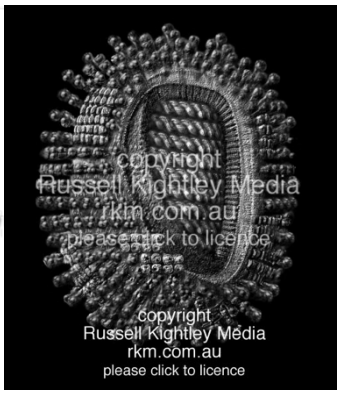
- Most viruses are icosahedral because it is the most efficient crystalline arrangement for a small unit that contains enough genetic material to reproduce. It is also easily transported in water-based fluids.

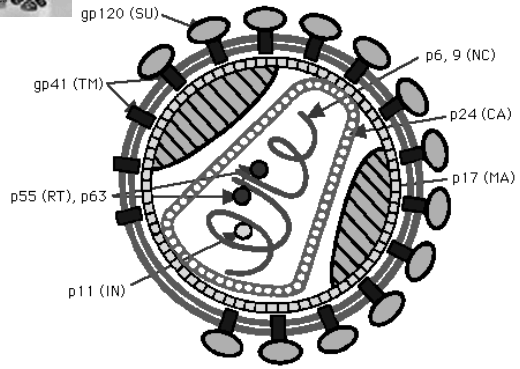
DNA & RNA: Examples of Viruses

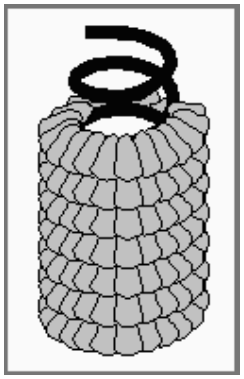






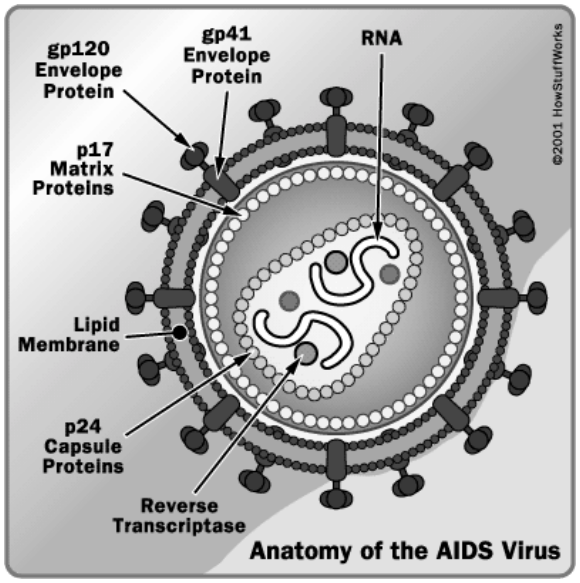






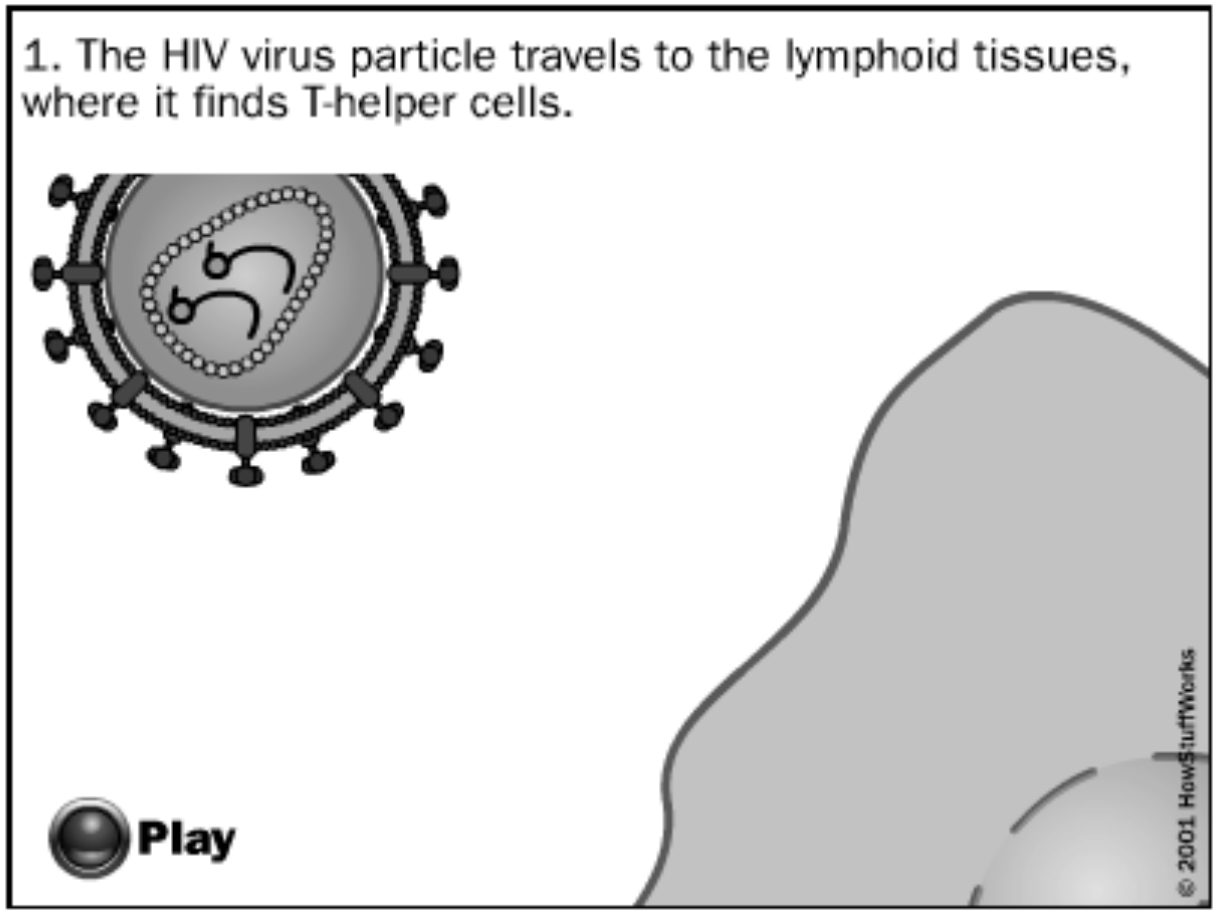
- DNA virus bacteriophage P22 infects *E. coli* (Left);
- Mostly RNA virions that infect animals and plants (Right): in humans: cold virus, herpes virus (a DNA virus), polio virus, influenza virus, HIV (a retrovirus); in plants (Far rt.): Tobacco Mosaic Rod Virus.

Human Immunodeficiency Virus (HIV): The Cause of AIDS

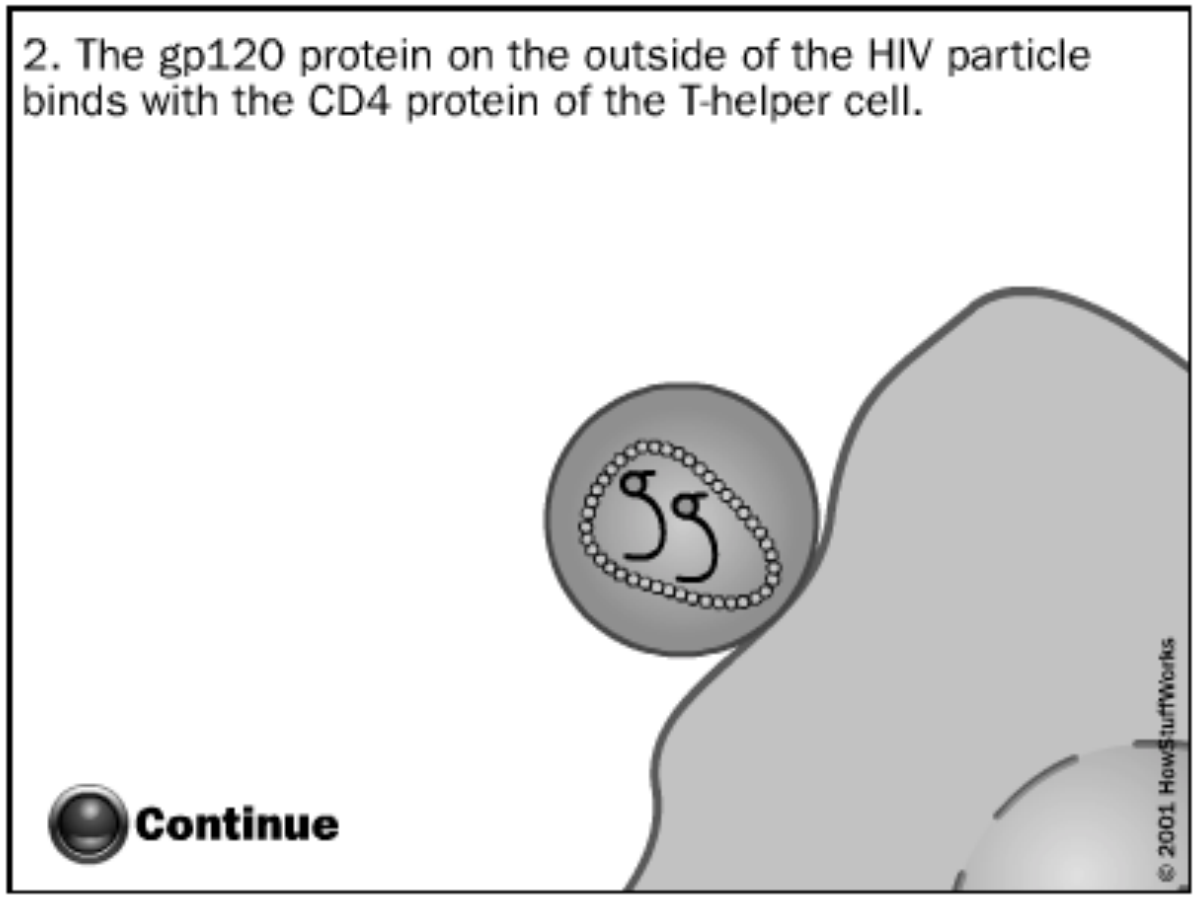


The structure of HIV is at left, and we see it infecting a human cell at right; it will ultimately cause Acquired Immune Deficiency Syndrome (AIDS).

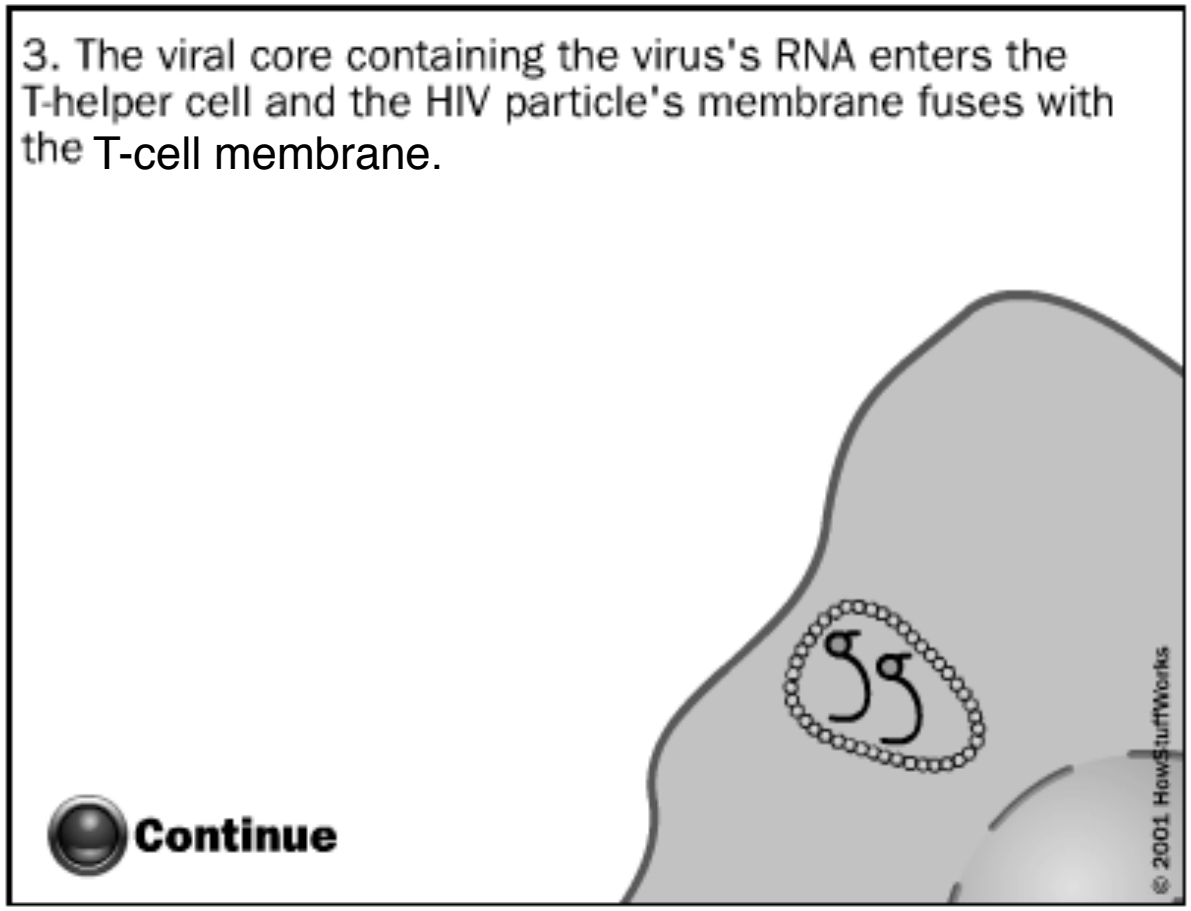
Step 1: HIV targets T-cells to infect.



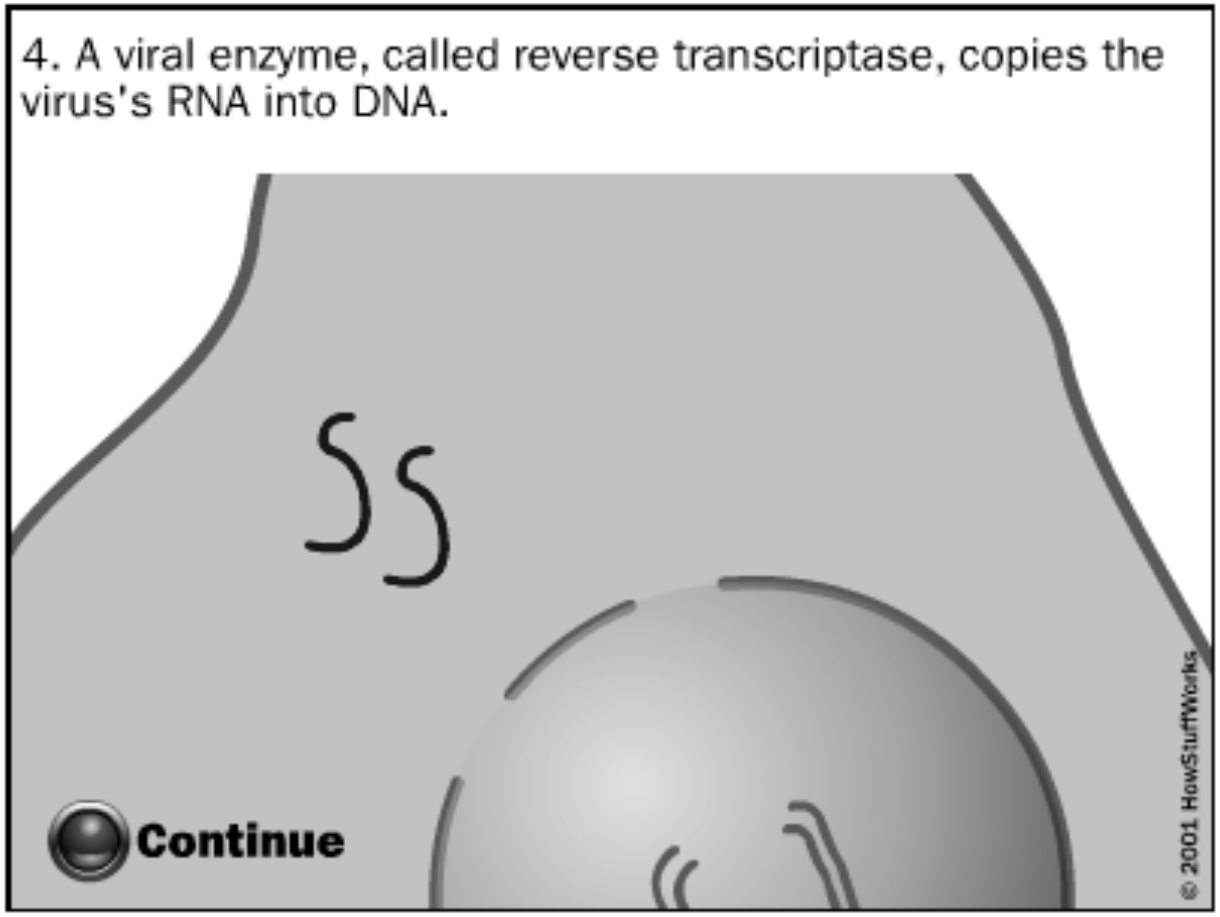
Step 2: HIV gp120 binds T-cell CD4.



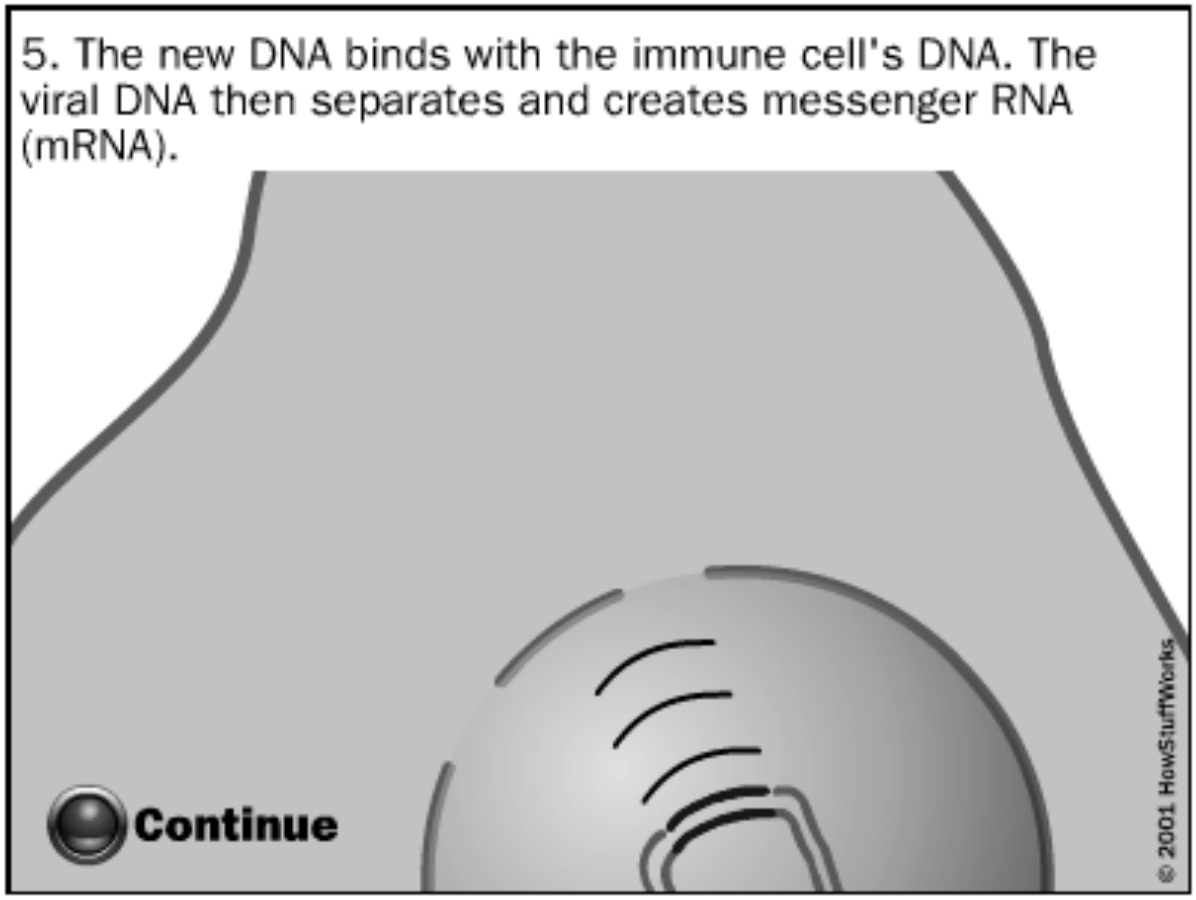
Step 3: HIV inserts RNA(black).



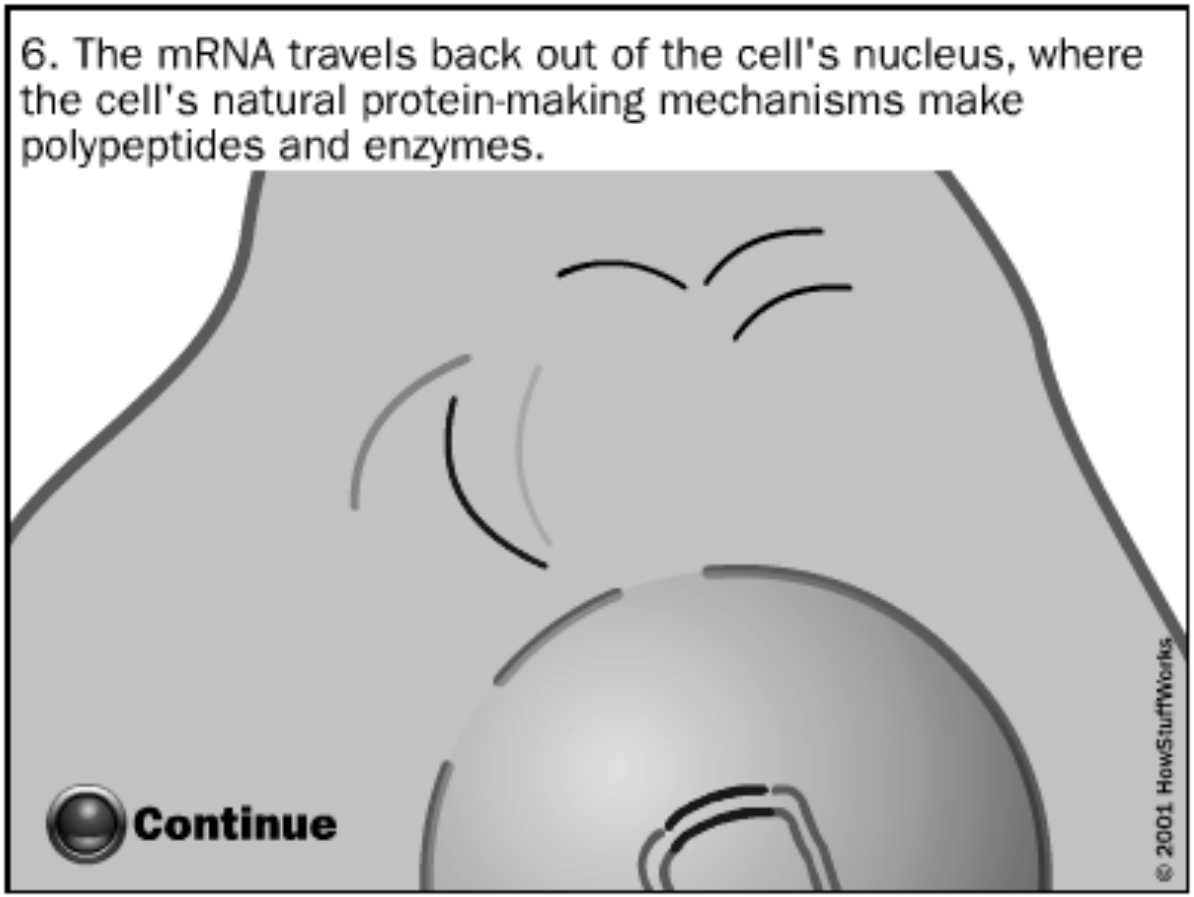
Step 4: Reverse Transcriptase copies RNA to DNA (blue).



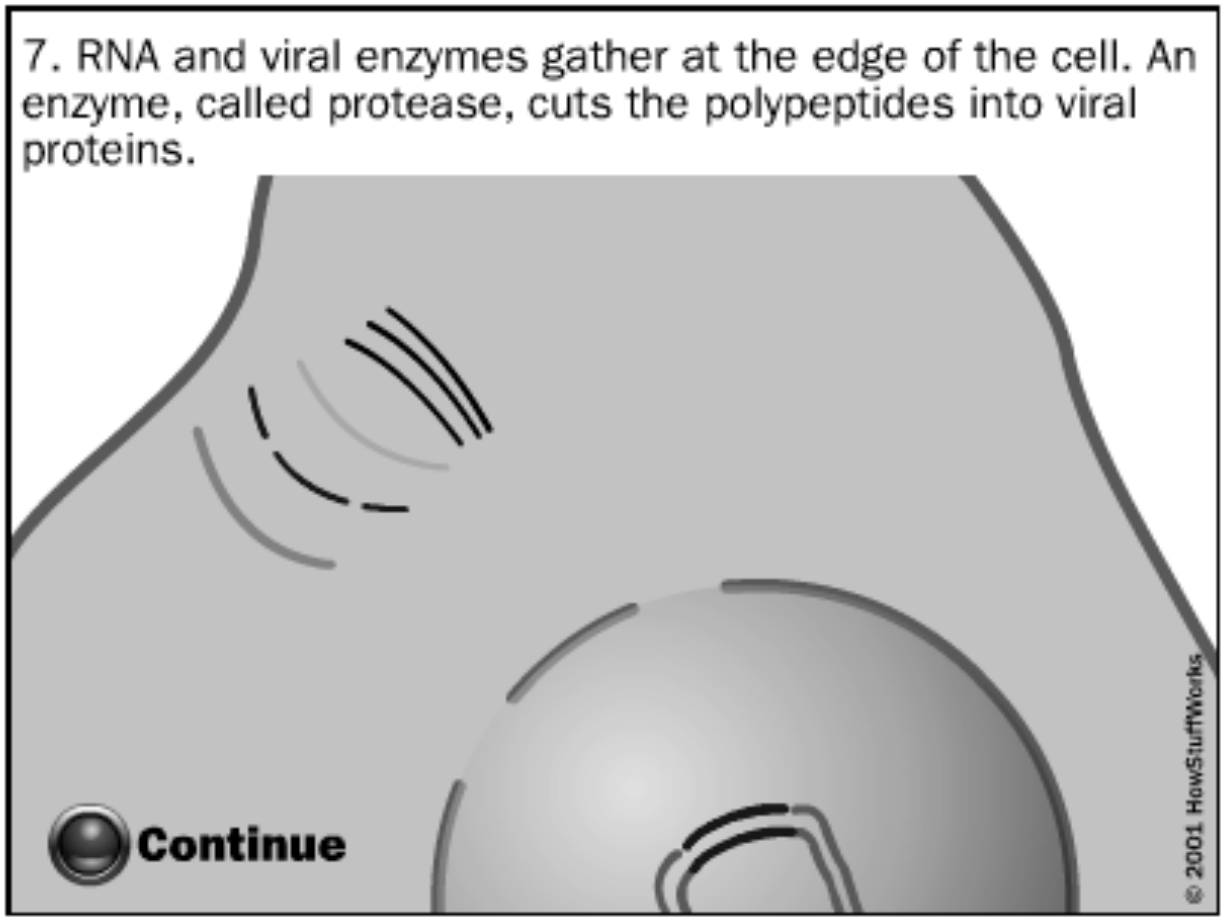
Step 5: DNA enters nucleus; makes mRNA to encode HIV.



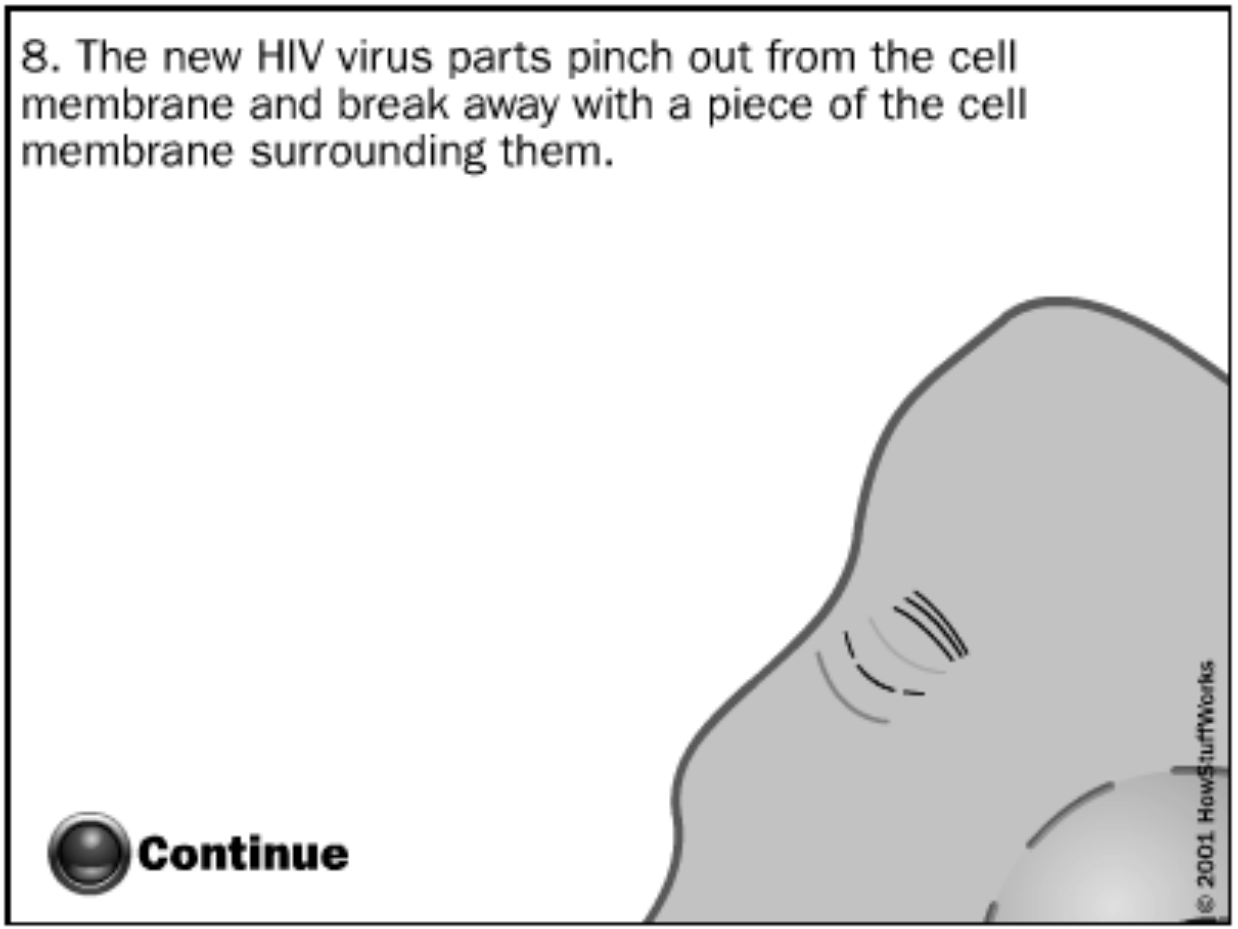
Step 6: mRNA enters cytoplasm to make polypeptides (colors).



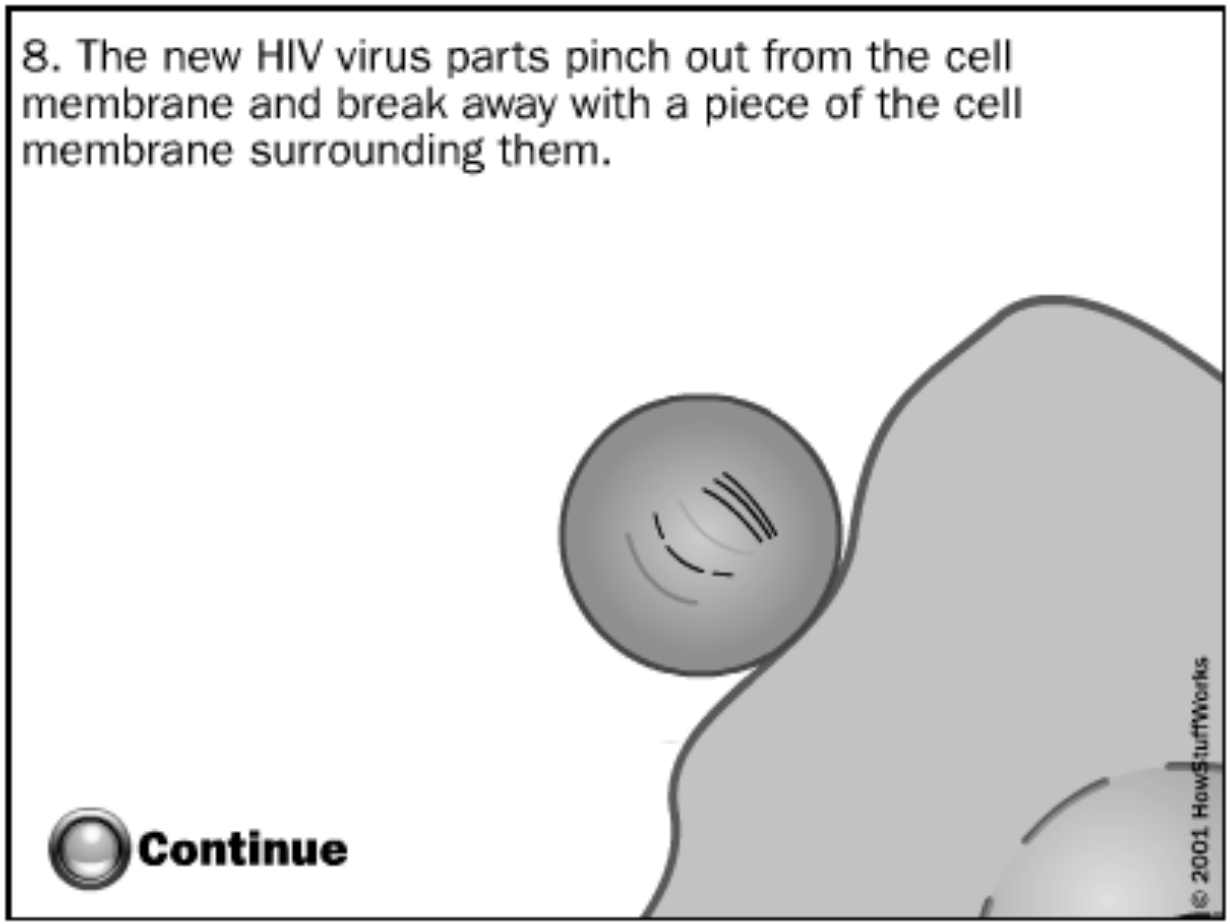
Step 7: HIV protease (green) cuts and creates viral proteins.



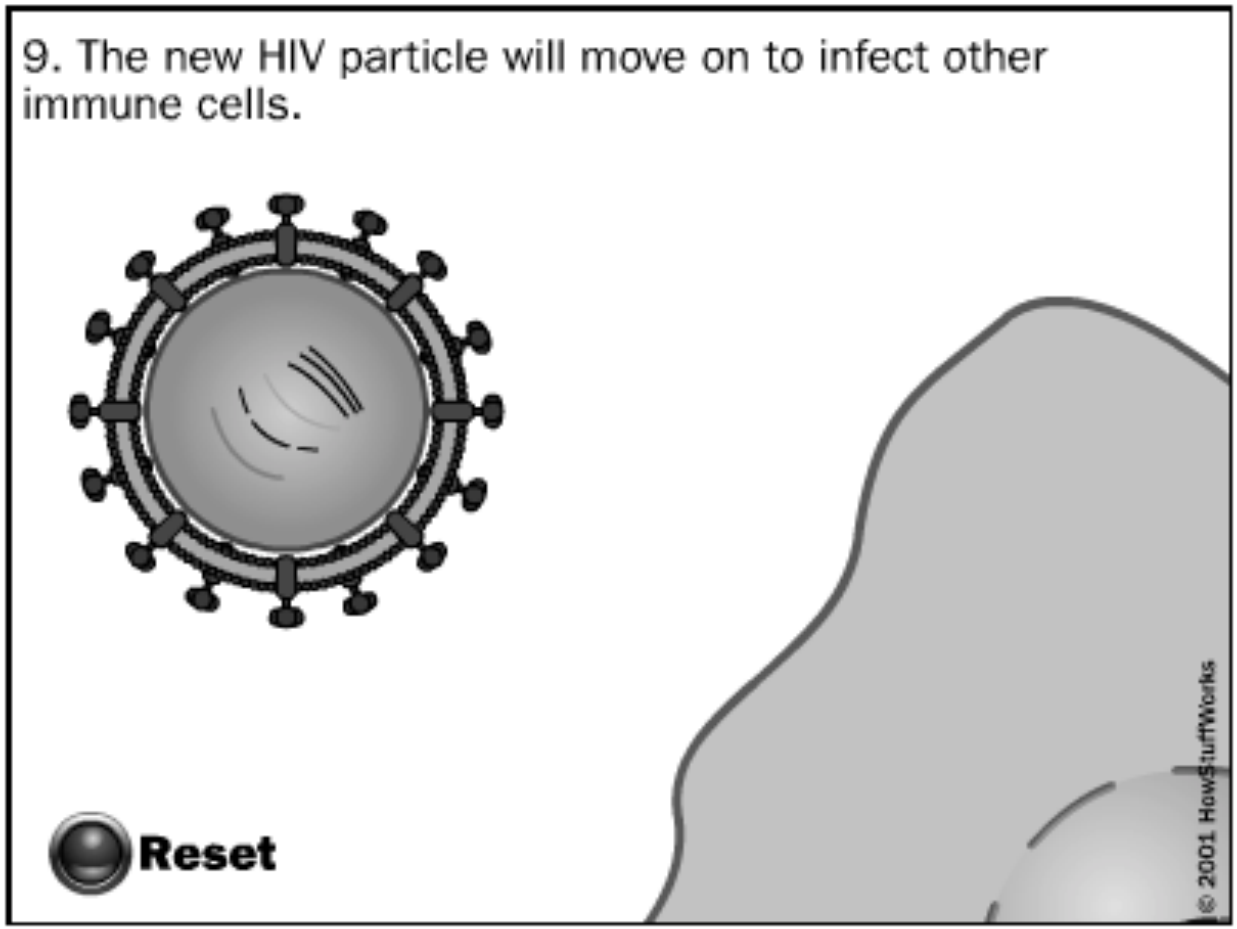
Step 8: HIV prepares to pinch out and break away from cell.



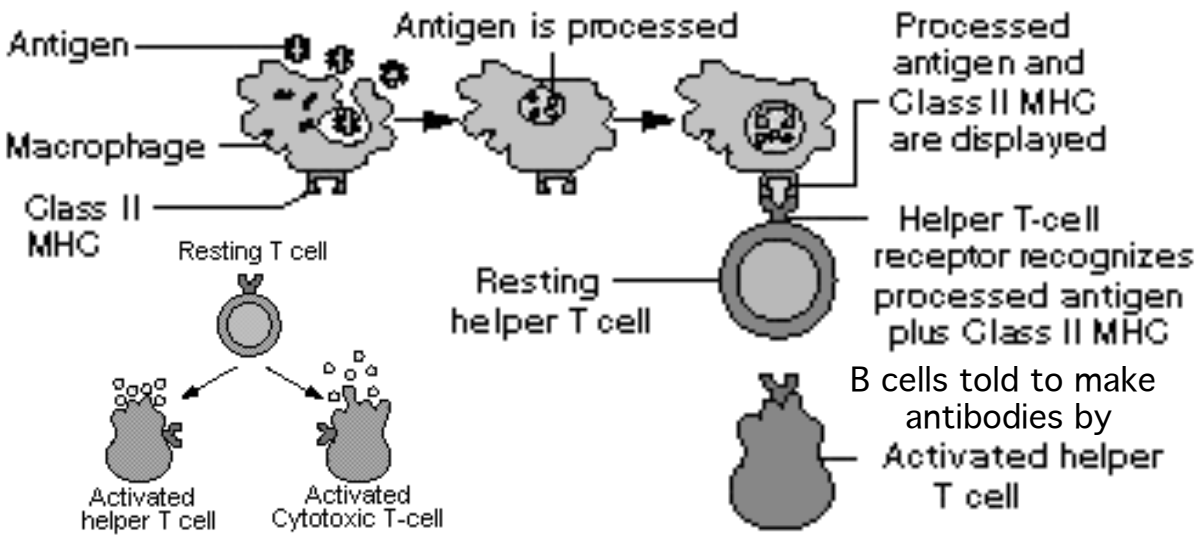
Step 9: HIV pinches out of cell.

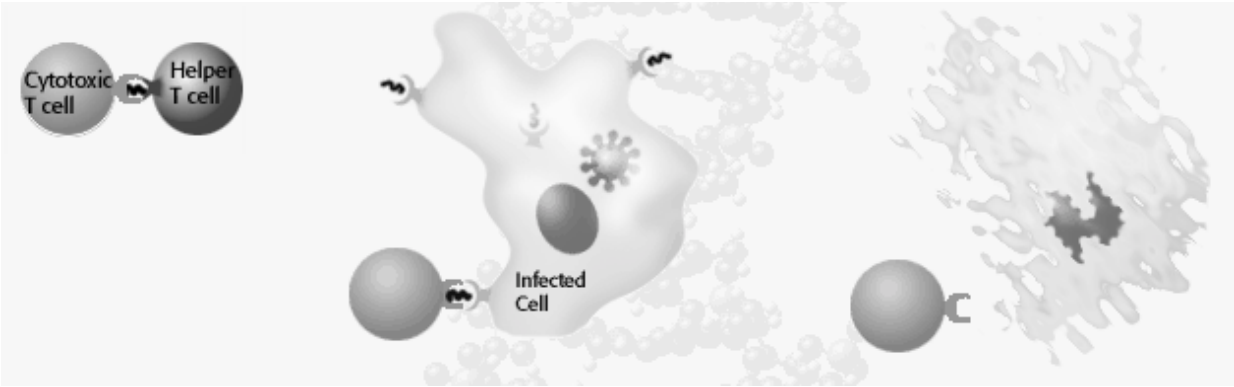


Step 10: Mature HIV emerges and infects other T-helper cells.



HIV and T-cells: Immunity Explained





Cytotoxic T Lymphocytes (CTL's) destroy invading microbes.

- Once the HIV virus enters the body, it heads for the lymphoid tissues, where it finds T-helper cells via binding CD4 and kills them: HIV is the only known human retrovirus that targets immune cells specifically. If helper T's die then killer T's cannot be made and do their job (see left).
- The newly replicated virions will infect other T-helper cells and cause the person's T-cell count to slowly dwindle by removing both the helper T cells and ultimately the CTL's that talk to them. The lack of T-helper cells compromises human immunity by preventing the removal of other harmful antigens with antibodies made by B cells (see left).
- No one dies from AIDS or HIV specifically. Instead, an AIDS-infected person dies from secondary infections, because his or her immune system has been dissipated. The loss of T-cells is the key to the loss of immunity.

Recent Trends in HIV/AIDS Infection

Epidemiology of HIV/AIDS in the United States

HIV InSite Knowledge Base Chapter
Published March 2003

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http://hivinsite.ucsf.edu/InSite?page=kb-01-03

Table 2. Distributions of U.S. AIDS Cases* by Transmission Exposure Group over Time

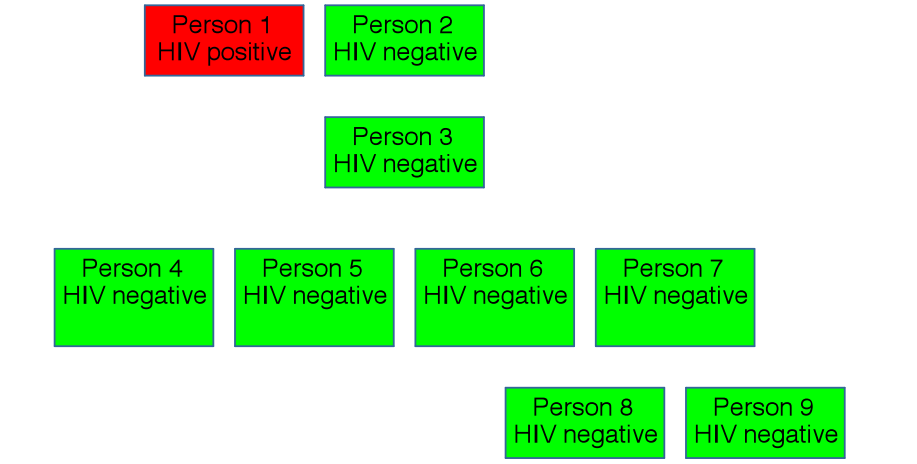
	Percent in Exposure Group		
Transmission Exposure Group	**1983**	**1992**	**2001**
MSM	71%	52%	40%
IDU	17%	25%	26%
MSM IDU	NA	5%	4%
Heterosexual contact#	5%	9%	28%
Blood/blood product recipient	2%	1%	0%
No risk identified/other	6%	6%	2%

Key
IDU: Injecting drug user
MSM: Men who have sex with men
NA: Not available

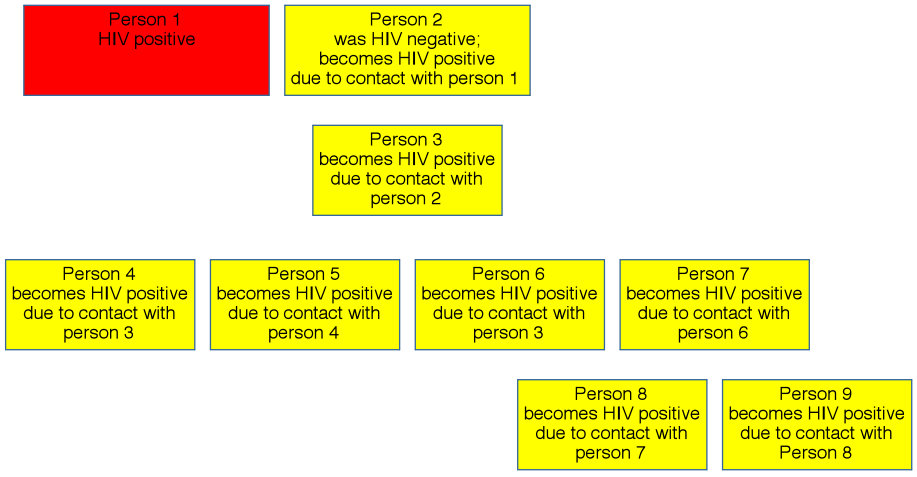
* Adult incident cases in 2001 adjusted for reporting delays and redistribution of cases initially reported with no risk identified (31% of reports in 2001).
\# Includes "Born out of United States," formerly a separate group in 1983 (4%).

- Heterosexual incidences of AIDS have ***INCREASED*** in the last 20 years, while other modes of transmission have leveled or decreased.
- Creates an epidemic.
- Why?
- Lack of Public Awareness.

HIV Transmission by Heterosexual Contact: a Geometric Expansion

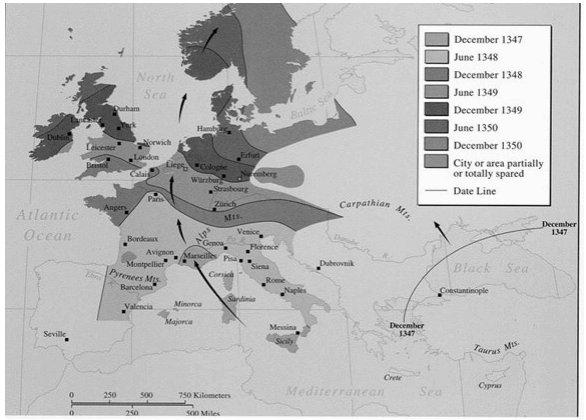


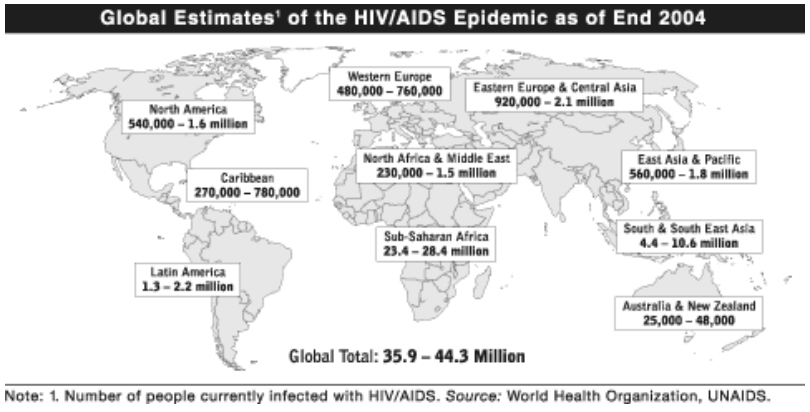
Before



After

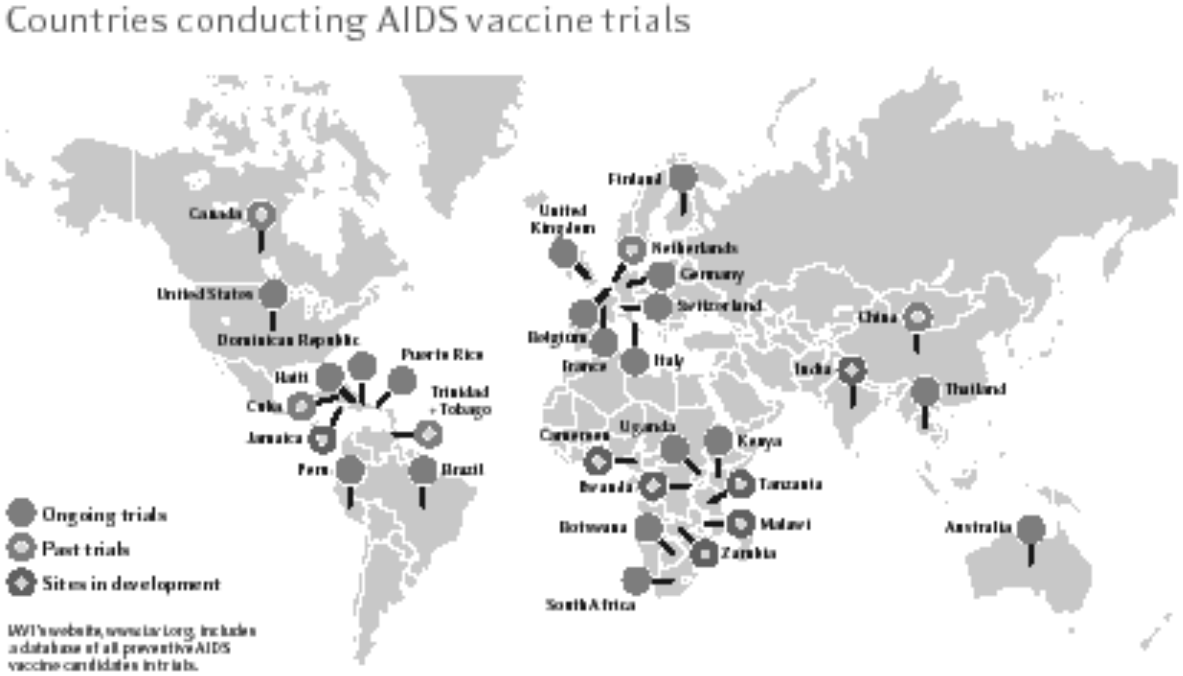
Evolutionary Adaptations Evade an Epidemic: Descendants of Plague Survivors Resist HIV





- CCR5 co-receptor enables certain microbes to invade immune cells by binding CD4 on helper T surface.
- *Yersinia pestis* bacterium causes Bubonic plague (Plague **Epidemic** of 1300: at left) by targeting T immune cells via CCR5.
- People missing CCR5 are resistant to plague and to HIV.
- We can treat plague today with antibiotics, but HIV is still untreatable (Current Worldwide HIV **Epidemic**: at left) because it evades the immune system and replicates rapidly under cover of the host cell.

Can There Be a Vaccine?



- Largest obstacles are financial and biological.
- Rapid mutation rates/different strains are a huge problem.
- Mechanism of HIV infection, which targets and depletes the immune system directly, is a huge hurdle.
- International AIDS Vaccine Initiative (IAVI) started trials in India on vaccine tgAAC09: targets reverse transcriptase and HIV gag & pro proteins in the most prevalent HIV subtype C.

Conclusions

- HIV belongs to a family of retroviruses that target human immune cells.
- HIV is unique in that it kills by weakening the immune system so secondary infection occurs.
- Heterosexual contact is a growing mode of HIV/ AIDS spread creating epidemics in society.
- Descendants of plague survivors (evolved to evade the 1300 epidemic) have immunity to HIV, which has a similar mechanism of infection to the plague.
- There is no simple HIV vaccine due to this virus being under cover of the human host cells and depleting the immune system.

Acknowledgements

IMAGES and Content Courtesy of:

- http://science.howstuffworks.com/virus-human.htm/printable
- http://www.enchantedlearning.com/math/geometry/solids/
- http://www.tulane.edu/~dmsander/WWW/335/335Structure.html
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