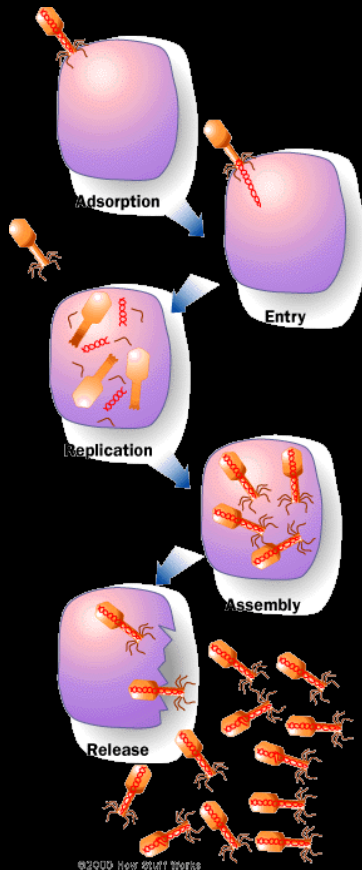


HIV Infection and Epidemiology: Can There Be a Cure?

Dr. Nedwidek

The Viral Life Cycle

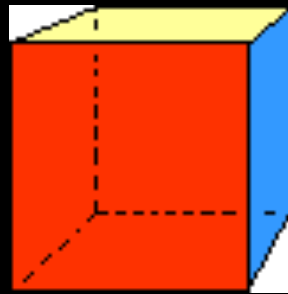


- A typical virus (DNA or RNA + protein) enters the host cell, makes more of itself, and exits.
- There are two major types of viruses: bacteriophage (left) infect prokaryotes, and other virions infect eukaryotes (animal or plant cells).

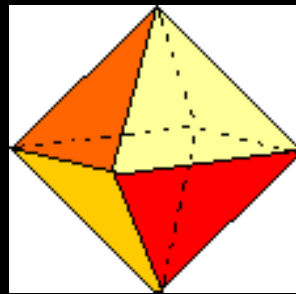
The Platonic Solids and Viruses



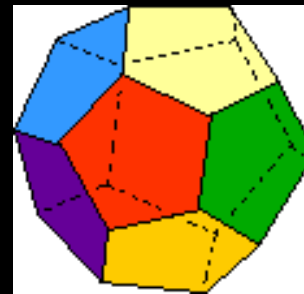
Tetrahedron



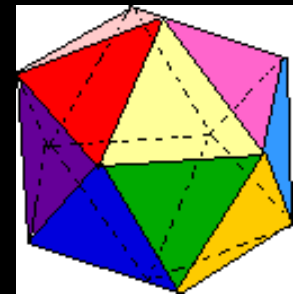
Cube



Octahedron



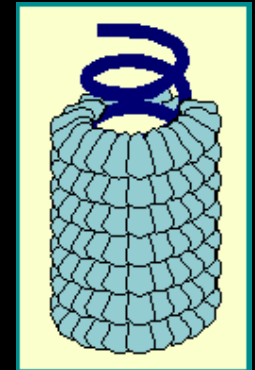
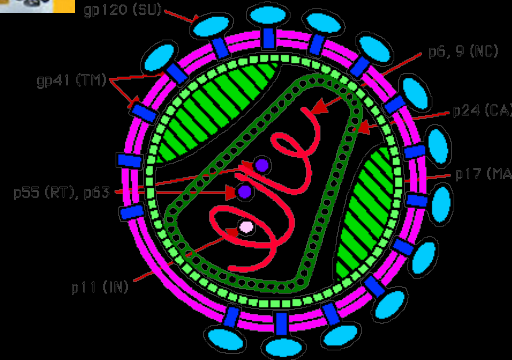
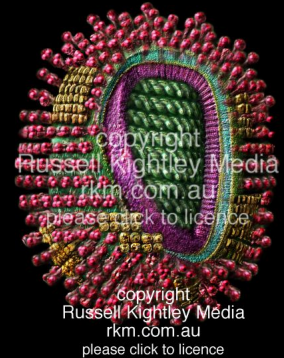
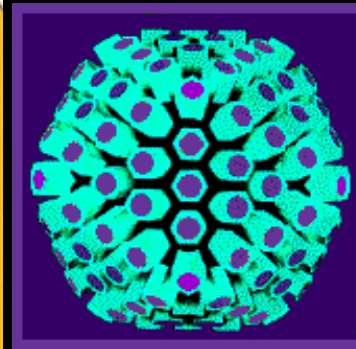
Dodecahedron



Icosahedron

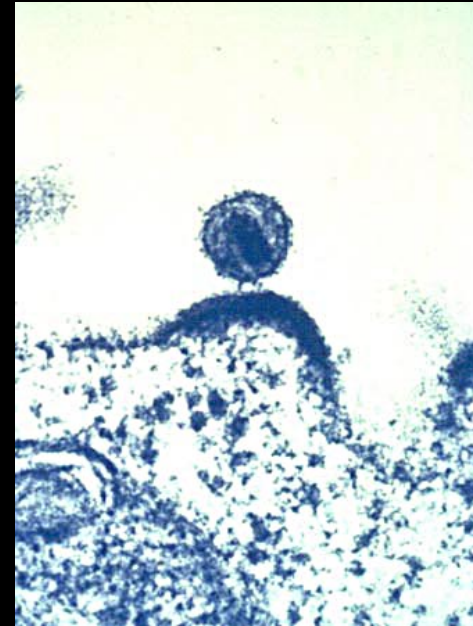
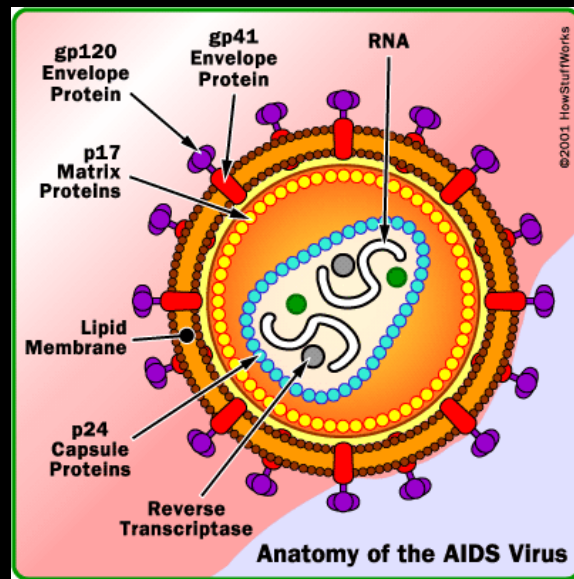
- Plato said that each of these 5 solids represented an “element” on earth: Tetrahedron for Fire, Cube for Earth, Octahedron for Air, Dodecahedron for the Cosmos, Icosahedron for Water.
- Most viruses are icosahedral because it is the most efficient crystalline arrangement for a small unit that contains 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.

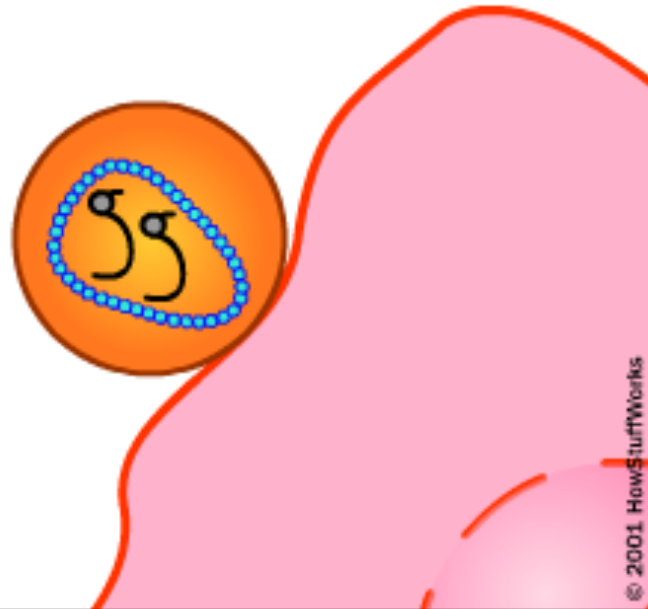
1. The HIV virus particle travels to the lymphoid tissues, where it finds T-helper cells.



© 2001 HowStuffWorks

Step 2: HIV gp120 binds T-cell CD4.

2. The gp120 protein on the outside of the HIV particle binds with the CD4 protein of the T-helper cell.



Continue

Step 3: HIV inserts RNA(black).

3. The viral core containing the virus's RNA enters the T-helper cell and the HIV particle's membrane fuses with the T-cell membrane.



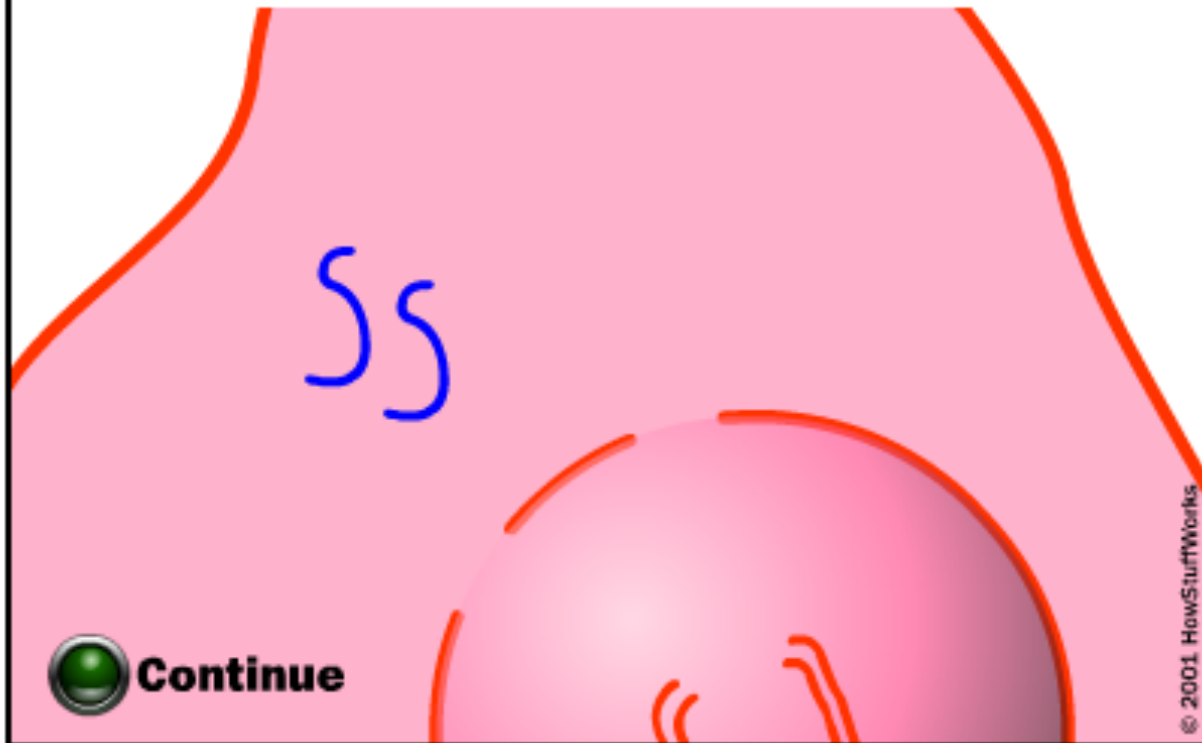
Continue



© 2001 HowStuffWorks

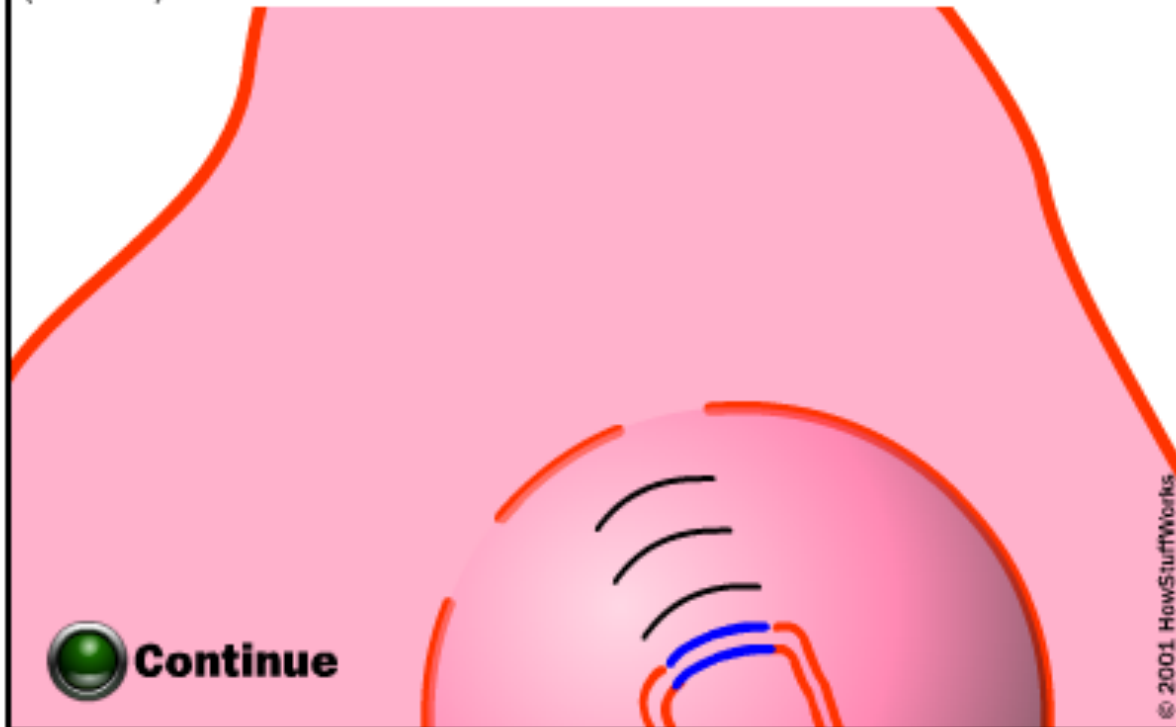
Step 4: Reverse Transcriptase copies RNA to DNA (blue).

4. A viral enzyme, called reverse transcriptase, copies the virus's RNA into DNA.



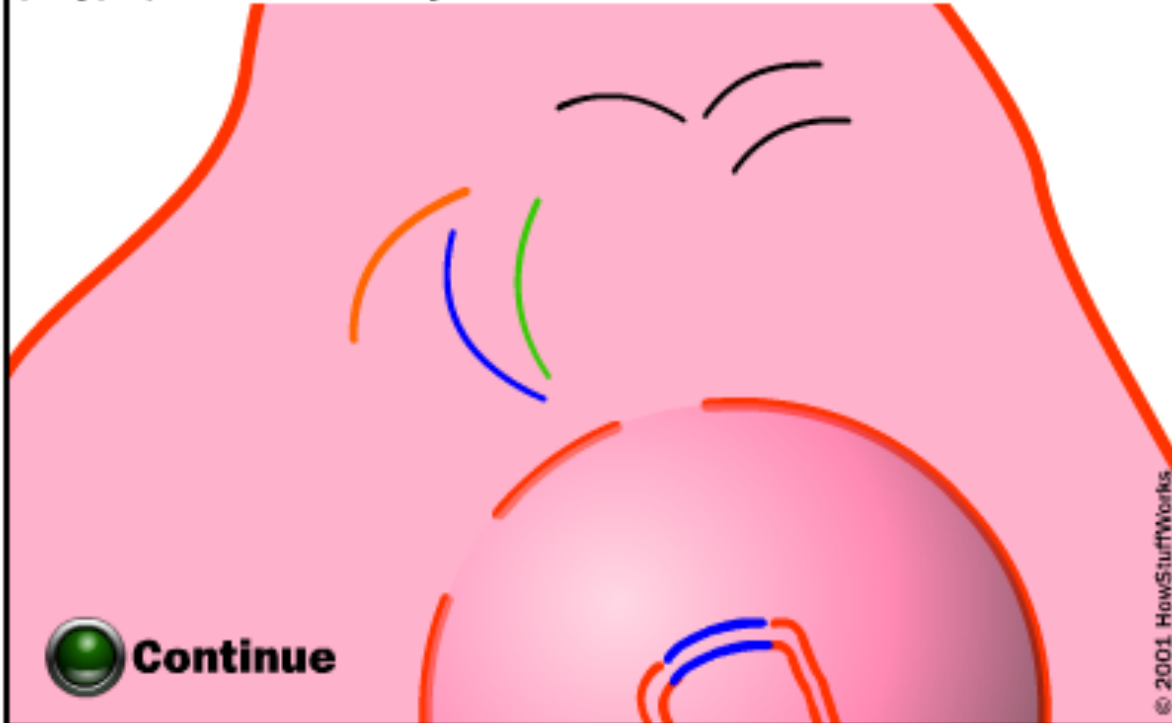
Step 5: DNA enters nucleus; makes mRNA to encode HIV.

5. The new DNA binds with the immune cell's DNA. The viral DNA then separates and creates messenger RNA (mRNA).



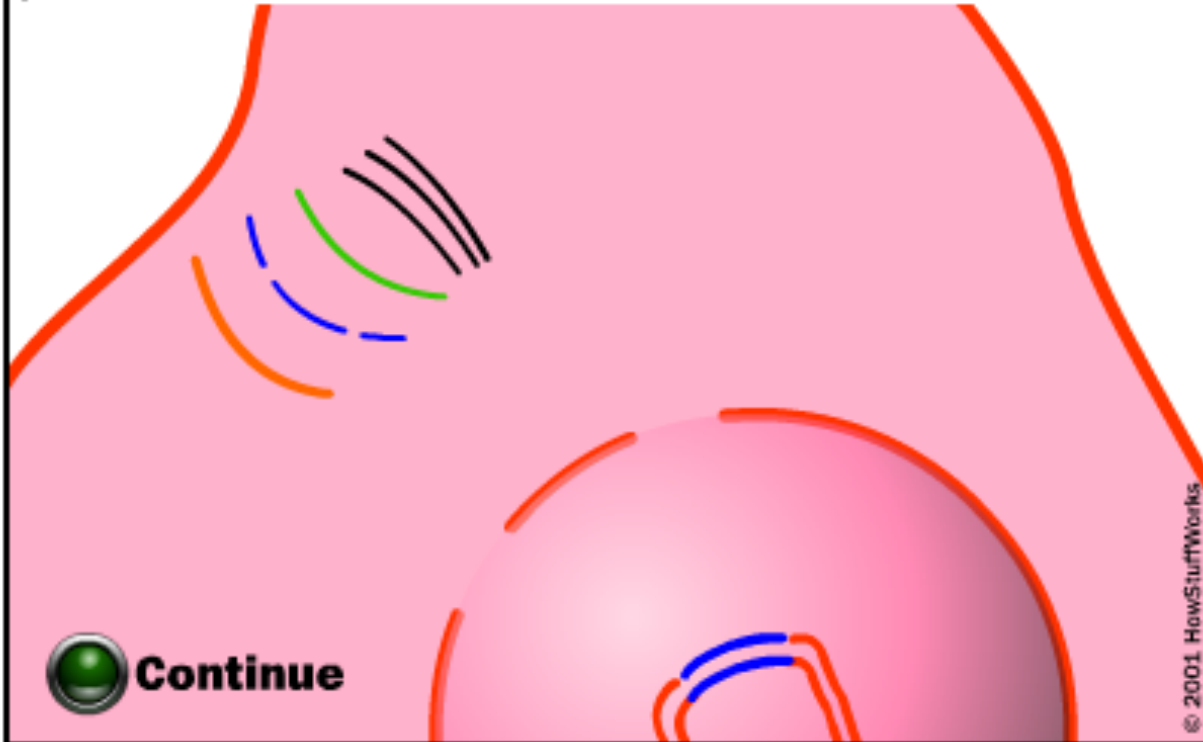
Step 6: mRNA enters cytoplasm to make polypeptides (colors).

6. The mRNA travels back out of the cell's nucleus, where the cell's natural protein-making mechanisms make polypeptides and enzymes.



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

7. RNA and viral enzymes gather at the edge of the cell. An enzyme, called protease, cuts the polypeptides into viral proteins.



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

8. The new HIV virus parts pinch out from the cell membrane and break away with a piece of the cell membrane surrounding them.



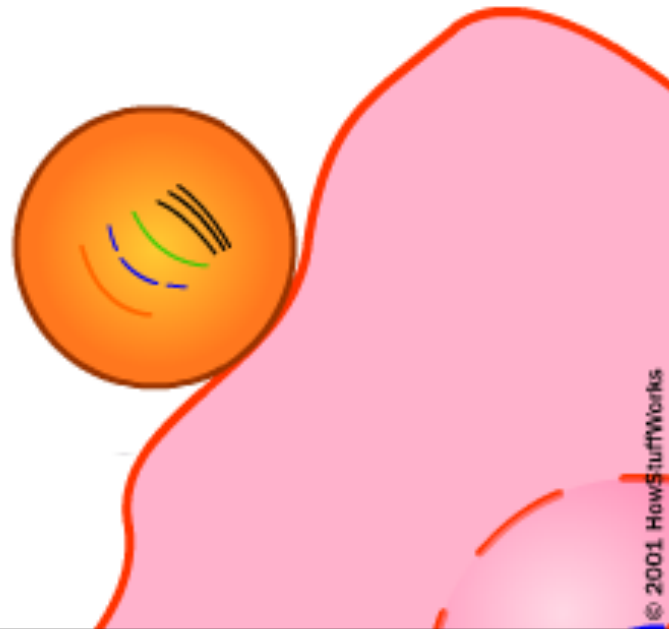
Continue



© 2001 HowStuffWorks

Step 9: HIV pinches out of cell.

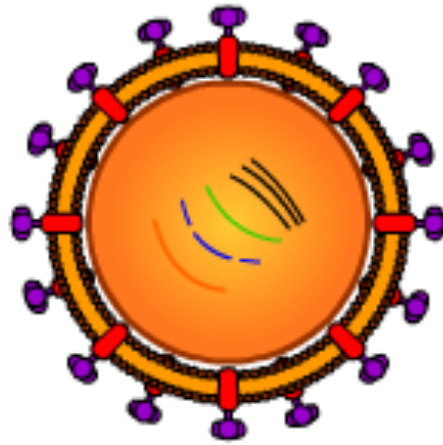
8. The new HIV virus parts pinch out from the cell membrane and break away with a piece of the cell membrane surrounding them.



Continue

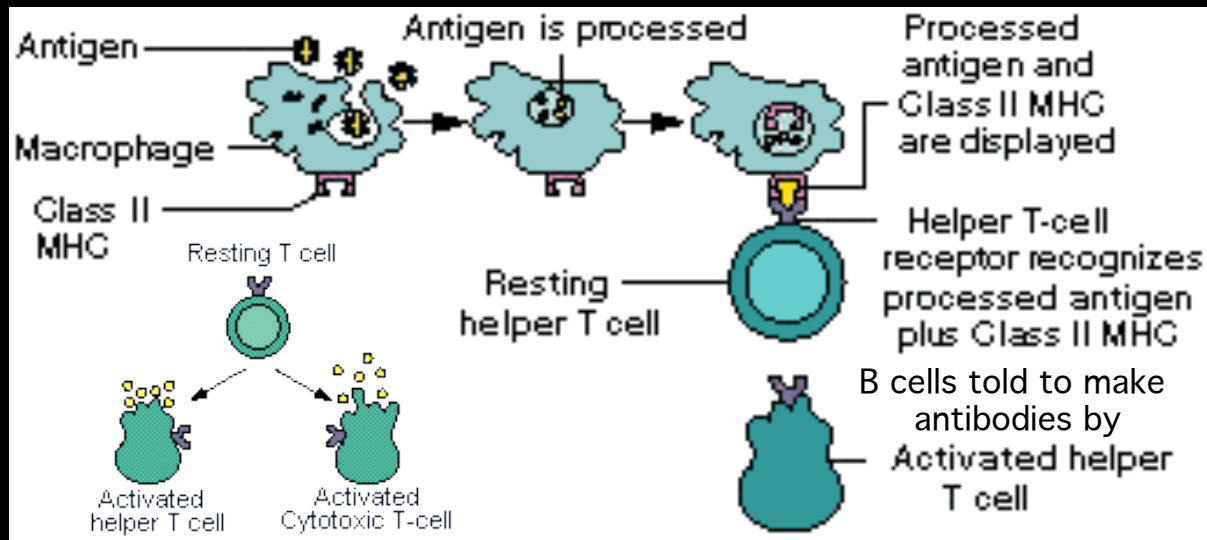
Step 10: Mature HIV emerges and infects other T-helper cells.

9. The new HIV particle will move on to infect other immune cells.

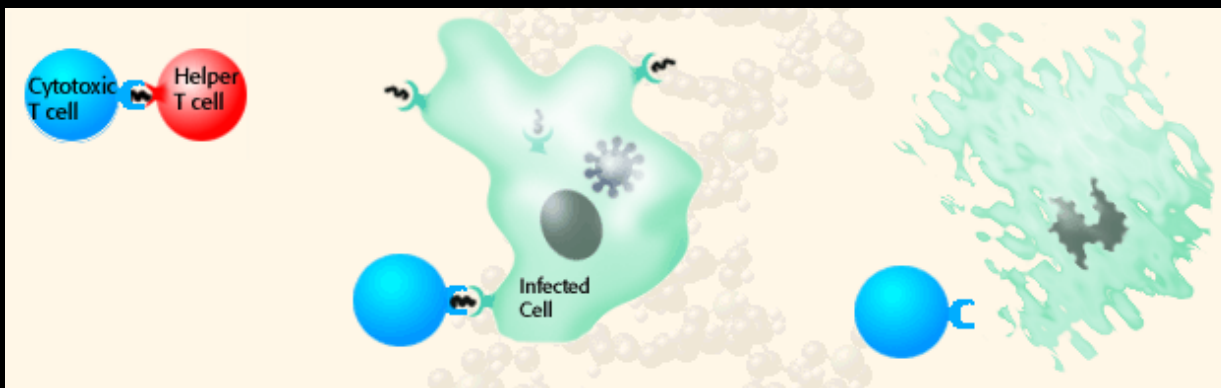


© 2001 HowStuffWorks

HIV and T-cells: Immunity Explained



- 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.



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

Recent Trends in HIV/AIDS Infection

Epidemiology of HIV/AIDS in the United States

HIV InSite Knowledge Base Chapter
Published March 2003

Dennis H. Osmond, PhD, University of California San Francisco
<http://hivinsite.ucsf.edu/InSite?page=kb-01-03>

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

| Transmission Exposure Group | Percent in 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

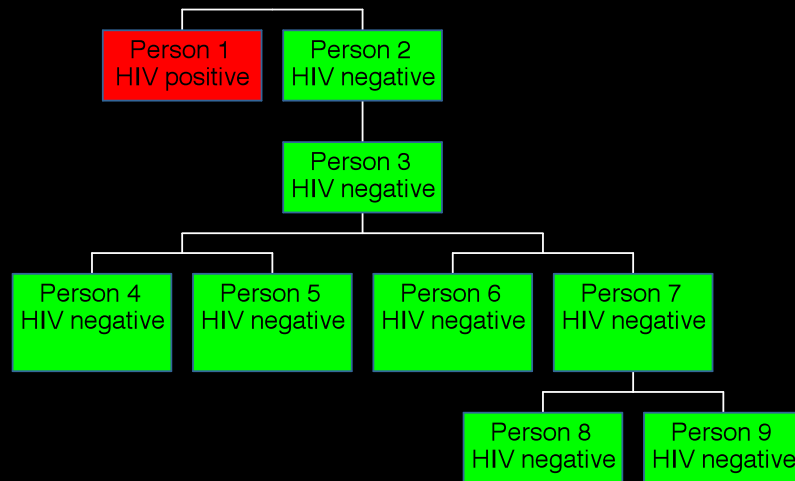
IDU: Injecting drug user
MSM: Men who have sex with men
NA: Not available

* Adult incident cases in 2001 adjusted for reporting delays and redistribution of cases initially reported with no risk identified (31% of reports in 2001).

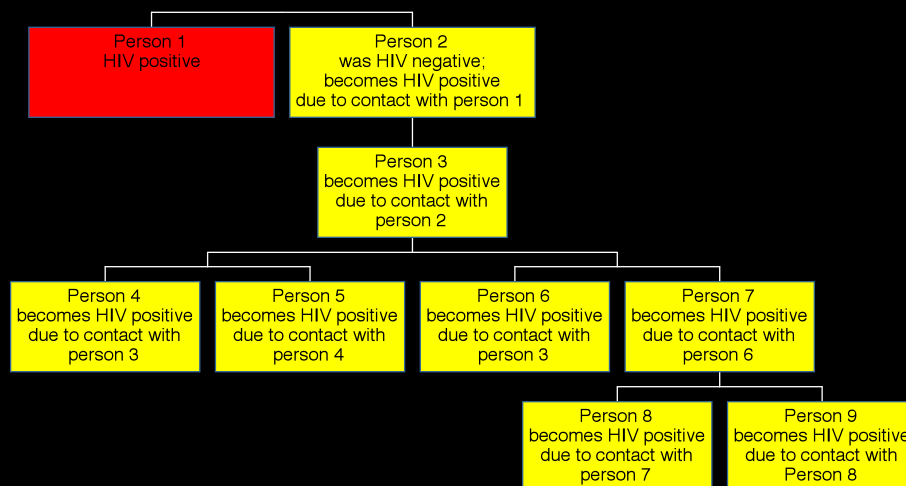
Includes "Born out of United States," formerly a separate group in 1983 (4%).

- 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

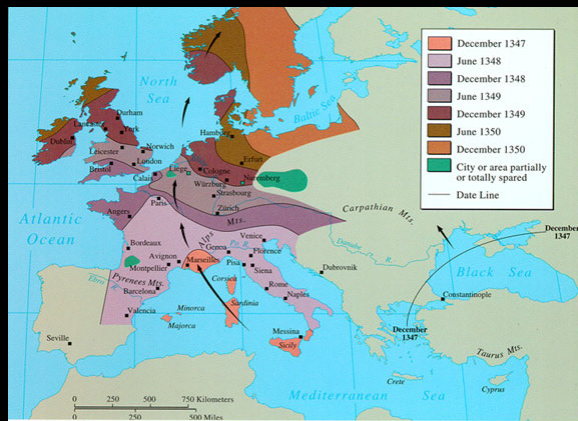


Before

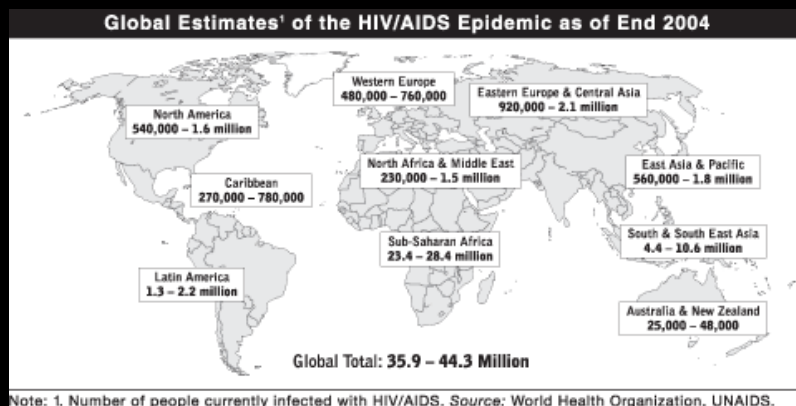


After

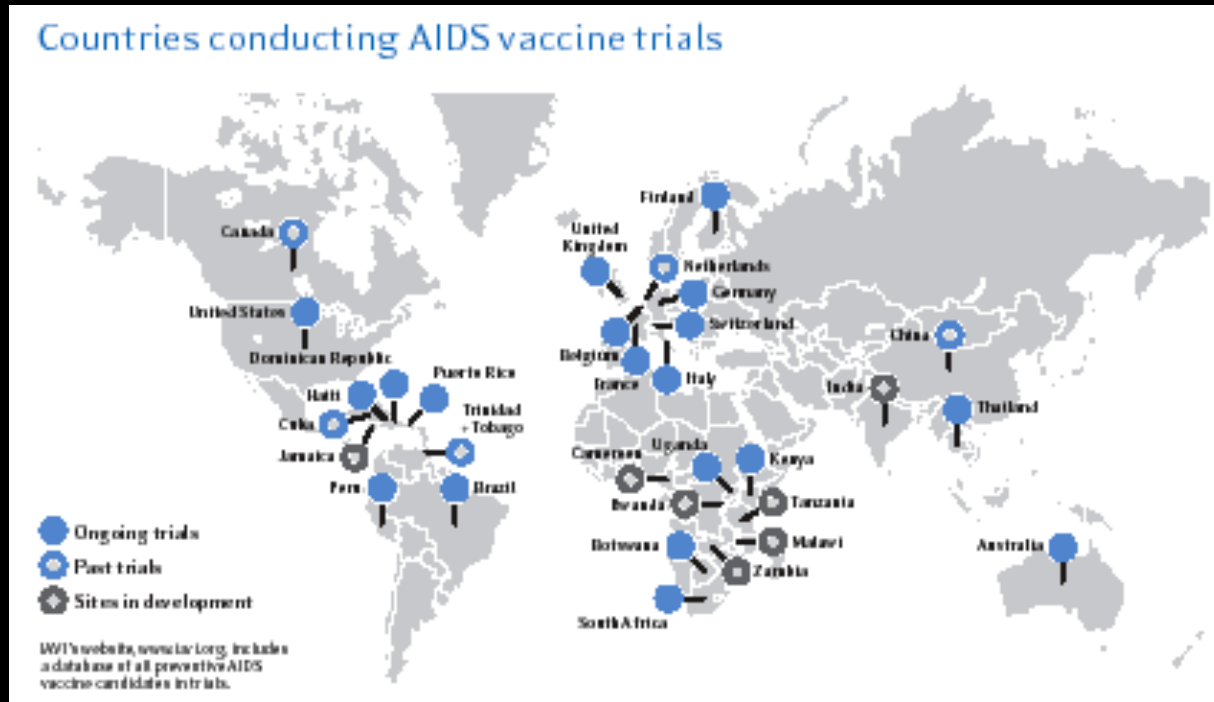
Evolutionary Adaptations Evade an Epidemic: Descendants of Plague Survivors Resist HIV



- 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>
- <http://www.rkm.com.au/VIRUS/BACTERIOPHAGE/phage-p22-virion.html>
- <http://www.rkm.com.au/VIRUS/Influenza/flu-structure.html>
- <http://web.uct.ac.za/depts/mmi/stannard/virarch.html>
- <http://health.howstuffworks.com/aids.htm>
- <http://health.howstuffworks.com/aids4.htm>
- <http://health.howstuffworks.com/framed.htm?parent=immune-system.htm&url=http://www.niaid.nih.gov/final/immun/immun.htm>
- <http://www.biology.arizona.edu/immunology/tutorials/AIDS/response.html>
- <http://hivinsite.ucsf.edu/InSite-KB-ref.jsp?page=kb-01-03&ref=kb-01-03-tb-02&no=2>
- <http://plagueyersiniapestis.homestead.com/YERSINIAPESTIS.HTML>
- <http://www.factmonster.com/ipka/A0762277.html>
- <http://www.iavi.org/viewfile.cfm?fid=7574>
- <http://www.iavi.org/viewpage.cfm?aid=100>