


Viruses

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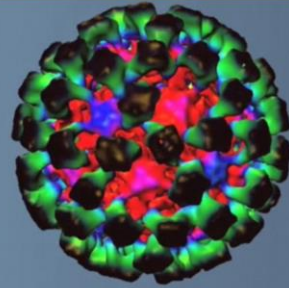
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Dougherty, M. & Chiu, W. (1996). *Viruses*. National Center for Macromolecular Imaging. Houston, Tx: Baylor College of Medicine.

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What are viruses?

- Viruses are major microscopic disease causing agents.
 - Depend on host to reproduce (parasites)
 - By understanding mechanisms of virus action, it is possible to control or minimize negative effects of viruses



CALICI



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Transcript from "Viruses," National Center for Macromolecular Imaging

Viruses have always lived alongside us. They've killed many millions of us. Despite their enormous power to cause disease, they're dependent on us. Invisible and deceitful, viruses are microscopic parasites. Without a host, they cannot reproduce. As scientists discover the chemical rules by which each virus plays, they can control how a virus affects us.

Additional Virus information:

Calici viruses have been identified in humans, other primates, cattle, mink, swine, dogs, chickens, cats, and others. Calici

causes a common gastroenteritis that is rarely diagnosed due to lack of adequate laboratory tests. Symptoms include acute gastrointestinal problems with more vomiting than diarrhea. (CDC. *Foodborne illness*. Retrieved 03/12/2007 from Garry, R. *The big picture book of viruses*. Tulane University School of Medicine. Retrieved 7-11-2007 from http://www.tulane.edu/~dmsander/Big_Virology/BVRNAcalici.html)

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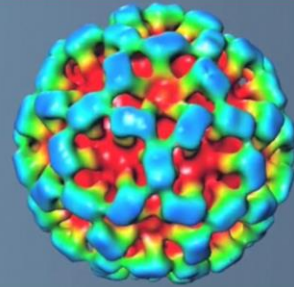
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Image Reference

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Virus – Etymology

- “Virus” is the Latin word for poisonous slime or ooze.
- Today also used to describe computer programs that “infect” and interfere with software functions.
- Different names are associated with virus in different settings:
 - Vector: viral genome that is engineered to serve as a tool to replicate and express genes.
 - Virion: the complete infectious virus particle



NORWALK



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Long ago, "virus" was the name for snake venom, from the Latin for a slimy liquid poison. Today, we also use the word to describe a certain kind of computer software. It makes sense. A software virus can poison healthy software.

Additional Virus information:

Norwalk causes outbreaks of diarrhea and viral gastroenteritis, most commonly among school-aged children. A common source for transmission of the virus is contaminated food or drinking water.

(U.S. National Library of Medicine. *Viral gastroenteritis*. NIH. Retrieved 03/12/2007 from <http://www.nlm.nih.gov/medlineplus/ency/article/000252.htm>)

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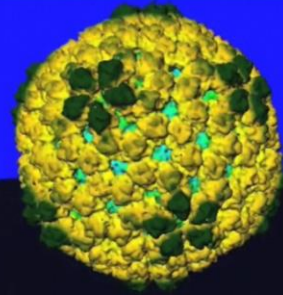
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Viruses – Size

- Smallest living entity capable of reproduction (within a host cell)
- Discovered in the 1890's
- Can be seen with an electron microscope



RICE DWARF



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Biological viruses were discovered about one hundred years ago. The invention of the electron microscope made them visible. Bacteria, much larger microorganisms, were seen 300 years earlier by the light microscope. Viruses are the smallest living entities that can reproduce.

Additional Virus information:

Rice Dwarf is one of the most economically damaging disease causing viruses of rice plants in Southeast Asia. Rice Dwarf virus belongs to the family Reoviridae, which also includes some viruses that infect the gastrointestinal tract. Rice Dwarf virus primarily is transmitted by leafhopper insects and can replicate in both its plant host and insect vector. Viruses in the family of Reoviridae live in a variety of plant, animal and insect hosts. Members of the family are varied in their structure but share similar replication mechanisms. (*International Committee on Taxonomy of Viruses*. Retrieved 7-11-2007 from <http://www.ncbi.nlm.nih.gov/ICTVdb/ICTVdB/00.060.0.08.001.htm>)

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Image Reference

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Viruses – Size

- Here is how you can imagine the size of viruses:
 - If a virus was the size of a basketball:
 - A bacterium would be as large as a city block
 - A grain of sand would be two miles long
 - A person would be 4,000 miles tall



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Transcript from “Viruses,” National Center for Macromolecular Imaging

Here is a way to imagine them. If a virus were the size of a basketball, a bacterium would be the size of a city block, a grain of sand would be two miles long, and a person would be 4,000 miles tall.

Reference

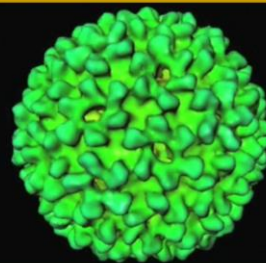
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Image Reference

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Viruses – History

- Invasions, wars, and immigrations can introduce viral diseases to different populations
- Some viral infections have had major global effects:
 - Influenza type A is believed to be responsible for global flu outbreaks in 1918, 1957 and 1968
 - 16th century Spanish explorers brought small pox, measles and influenza viruses to the New World



P22



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Transcript from “Viruses,” National Center for Macromolecular Imaging

Tiny but lethal, viruses have changed human history. In 1918, a worldwide influenza epidemic killed more than 20 million people within a few months. In the 16th century, Cortez and 600 soldiers invaded Mexico on horseback. The native Aztecs had never seen horses. Cortez also brought something Aztecs couldn't see, smallpox, measles and influenza viruses.

Additional Virus information:

This image of the *Salmonella* bacteriophage P22 was made using several different reconstruction methods. The *Salmonella* bacteriophage P22 has similar assembly and maturation steps as other phages and Herpesvirus.

References

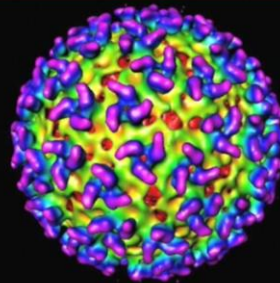
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Image Reference

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Viruses – Structural Biology

- The key to the success in the battle against viruses is understanding different viral mechanisms.
- Scientists study :
 - Viral structure
 - Viral life cycle
 - Mechanisms of cell infection
 - Viral replication
 - Host cellular proteins needed by the virus (used as antiviral targets)



SINDBIS



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Transcript from “Viruses,” National Center for Macromolecular Imaging

Structural biology is a branch of science fighting the war on viruses. Understanding how a virus lives and multiplies is the key to solutions that stop the chemical process the virus uses. Antiviral agents are one of the weapons in this war. Just as a bacterium in an infected cell absorbs antibiotics and dies, an antiviral agent is absorbed into the infected host cell. There, it destroys a unique chemical the virus needs; the virus is disabled.

Additional Virus information:

The *Sindbis* virus is a member of the *Togaviridae* that is spread by mosquitoes and replicates inside the host cell cytoplasm. These viruses have been used as vectors in biomedical research, for example to transfer genes into host cells.

References

Dougherty, M. & Chiu, W. (1996). *Viruses*. National Center for Macromolecular Imaging. Houston, Tx: Baylor College of Medicine.

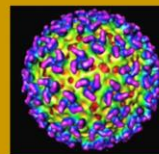
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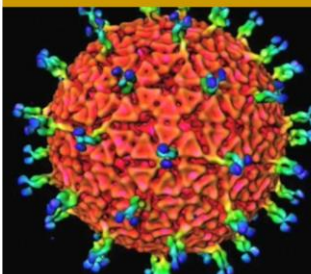
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Viruses – In Medicine

- Vaccines against viruses enhance the immune response of the host
 - Immune cells are exposed to viral proteins or deactivated virus
 - Immune system creates specific memories
 - Immune system is enhanced and “ready” to defend against the virus
- Scientists are investigating methods that use viruses for treatment of diseases such as cancer and Alzheimer's disease.



SINDBIS



ROTA



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Vaccines are a second antiviral weapon. A vaccine introduced into the body gives it a clue about its attacker. Now the body can successfully fight the virus because it knows its chemical name. Smallpox no longer exists because of a vaccine. More than ten human vaccines have been created. Researchers are working to create vaccines for two of today's deadliest viruses, HIV and Rota. Rotavirus causes the dysentery that kills millions of children in underdeveloped countries. The relentless quality of these viral parasites is also an opportunity. Scientists are looking for ways to use viruses to deliver genetic fixes to cancer cells and to brain cells damaged by Alzheimer's.

Additional Virus information:

Rota Virus is the leading cause of gastroenteritis in children, adults, and elderly patients in nursing homes. The virus generally is contracted through contact with contaminated food or water. (U.S. National Library of Medicine. *Viral gastroenteritis*. NIH. Retrieved 03/12/2007 from <http://www.nlm.nih.gov/medlineplus/ency/article/000252.htm>; CDC. Retrieved 7-11-2007 from <http://www.cdc.gov/rotavirus/>)

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Image Reference

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Houston, Tx: Baylor College of Medicine.

Viruses – Examples

- O’Nyong-Nyong
- Hepatitis
- Rabies
- Polio
- HIV
- Rota
- Sindbis
- Norwalk
- Calici
- Lassa
- Dengue
- Marburg
- Yellow-Fever
- Rubella
- Hantaan
- Epstein-Barr
- Cowpox
- Influenza
- Ebola
- OMSK
- Junin
- Duvenhage
- Oropouche
- ORF
- Coxsackie
- Chikungunya
- Bunyamwera
- Herpes



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Virologists have identified about 4,000 viruses. Viruses are different from bacteria, fungi, algae, plants and animals, but viruses are parasites to all of them. To copy themselves and grow, they must first infect and hijack a cell. It's their structure that makes it possible for them to steal the life from a cell and use it. Though mostly genetic material, viruses usually have other chemicals such as sugars, fats and proteins. Of the identified viruses, more than one thousand infect people.

Additional Virus information:

O’Nyong-Nyong, a member of Togaviridae family was initially isolated in Uganda in 1959. Mosquitoes are the carriers of this virus that leads to high fever, arthritis and rash. (McGill, P. E., & Njobvu, P. D. (2001) Rheumatology in Sub-Saharan Africa. *Clinical Rheumatology*, 20, 163-167)

Hepatitis A, B, and C: Hepatitis refers to many types of diseases that cause liver inflammation.

Hepatitis A is a virus transmitted through contaminated food or water or direct contact with a person who already is infected with the virus and is the mildest form of viral hepatitis infections. (U.S. National Library of Medicine. *Hepatitis A*. NIH. Retrieved 03-12-2007 from <http://www.nlm.nih.gov/medlineplus/ency/article/000278.htm>).

Hepatitis B is a virus that is transmitted by contacting blood and other body fluids from a person already infected with the virus. (U.S. National Library of Medicine. *Hepatitis B*. NIH. Retrieved 03-12-2007 from <http://www.nlm.nih.gov/medlineplus/ency/article/000279.htm>).

Hepatitis C is a virus that also is transmitted through body fluids and is the one of the leading causes for the need for a liver transplant in the United States. (U.S. National Library of Medicine. *Hepatitis C*. NIH. Retrieved 03-12-2007 from <http://www.nlm.nih.gov/medlineplus/ency/article/000284.htm>).

Rabies is a curable viral disease (caused by Rhabdoviruses) found in mammals that is usually transmitted through the bite of an infected animal. Most deaths associated with Rabies are due to failure to seek prompt medical attention. (CDC. *Rabies*. Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/dvrd/rabies/introduction/intro.htm>)

Polio, also known as Poliomyelitis, is caused by Poliovirus. Polio invades the nervous system and may lead to paralysis. Transmission occurs by person-to-person contact, often via a fecal-oral or oral-oral route. (CDC. *Poliomyelitis*. Retrieved 03-13-2007 from <http://www.cdc.gov/nip/publications/pink/polio.pdf>)

Human immunodeficiency virus (HIV) is transmitted by contact with bodily fluids from an infected person. HIV destroys specific cells that are important for normal function of the immune system, often, but not always, resulting in the development of Acquired Immunodeficiency Syndrome (AIDS). (CDC. *HIV/AIDS*. Retrieved 03-19-07 from <http://www.cdc.gov/hiv/resources/>)

Lassa Fever is an acute viral infection named after the town in Nigeria where the first cases were discovered in 1969. Although it can be spread from person-to-person, the primary host is the *Mastomys* rodent (multimammate rat). These rodents are often found in human homes, greatly increasing the chance of passing the virus from rodent to humans. (CDC. *Lassa fever*. Retrieved 03-13-2007 from <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/lassaf.htm>)

Dengue fever is a mosquito-borne disease that can be caused by four different Dengue virus serotypes. The illness can result in a range of clinical syndromes from mild to severe and can be fatal. A person cannot infect another person. (CDC. *Dengue fever*. Retrieved 03-21-2007 from <http://www.cdc.gov/ncidod/dvbid/dengue/facts.htm>)

Marburg causes a rare, but severe, hemorrhagic fever in humans and primates. This virus is in the same family as Ebola virus. The first outbreak in 1967 resulted from exposure to African Green Monkeys and their tissue. The monkeys had been imported to Marburg, Germany, for research purposes and for use in preparing polio vaccine. (CDC. *Questions and answers about Marburg hemorrhagic fever*. Retrieved 03-13-2007 from <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/marburg/qa.htm>)

Yellow Fever is caused by a virus (in the *flavivirus* group) that is transmitted to humans through the bite of a female mosquito of several species. The disease only occurs in Africa and South America. Travelers to these regions are required to be vaccinated. (CDC. *Yellow fever: Disease and vaccine*. Retrieved 03-21-2007 from <http://www.cdc.gov/ncidod/dvbid/yellowfever/index.htm>, and <http://www.who.int/mediacentre/factsheets/fs100/en/>)

Rubella or German Measles is a viral disease that causes acute fever and rash in the infected individual. Rubella can be transmitted by a cough or sneeze of an infected person. The vaccine for the virus is included in the MMR immunization. (CDC. *Rubella: In short*. Retrieved 03-19-2007 from

<http://www.cdc.gov/nip/diseases/rubella/vac-chart.htm>)

Mumps, caused by a paramyxovirus, is an acute viral disease resulting in fever, muscle ache, and swelling of salivary glands. It is transmitted by direct contact with saliva or respiratory secretions of an infected individual. The vaccine for the Mumps virus is included in the MMR immunization. (CDC. *Mumps*. Retrieved 07-25-2007 from <http://www.cdc.gov/vaccines/vpd-vac/mumps/in-short-adult.htm>)

Measles is a highly contagious viral disease characterized by a red, blotchy rash. The vaccine for the Measles virus is included in the MMR immunization. While no longer common in the United States, travelers need to be aware that measles is a common disease in many countries. (CDC. (2005). *Measles. Traveler's Health: Yellow Book 2005-2006*. Retrieved 03-13-2007 from <http://www2.ncid.cdc.gov/travel/yb/utills/ybGet.asp?section=dis&obj=measles.htm>)

Hantaan is a viral disease transmitted by rats that causes "hemorrhagic fever with renal syndrome" (HFRS). Common in Asia, particularly in Korea, more than 2000 cases were reported during the Korean war among the United Nations troops. Since urban rats may often be infected with the virus, it is thought that ships harboring rats caused world wide dispersal of the virus. (Brooks, G. F., Butel, J. S., & Morse, S. A. (2004). *Jawetz, Melnick, & Adelberg's medical microbiology* (23rd ed.). McGraw-Hill.)

Epstein Barr, EBV, or Epstein Barr Virus, is considered the most common human virus, infecting most people at some point in their lives. It is found worldwide. EBV is the cause of infectious mononucleosis in adolescents and young adults. Once infected, EBV will establish a dormant infection. Rarely, it can play a role in the emergence of Burkitt's lymphoma and nasopharyngeal carcinoma. Transmission of EBV requires contact with the saliva of a person who is infected while the virus is in its active form. Epstein-Barr Virus is grouped as a member of the Herpesviridae family (CDC. *Epstein-Barr virus and infectious mononucleosis*. Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/diseases/ebv.htm>)

Cowpox is a viral skin disease that is very rarely seen today in humans. In 1798, Edward Jenner used cowpox to create the first immunization to smallpox (a related disease) by scratching the fluid from cowpox sores into the skin of healthy people. Jenner noticed that people who had been infected with cowpox were not only immune to further infections by cowpox, but also, to smallpox. (Levin, N. A. (2007).

Influenza virus cause respiratory infections that range from mild to severe and can lead to death. Typically spread from human-to-human, influenza is combated each year through vaccines prepared to match viral strains predicted to be prevalent during the coming year. (CDC. *Influenza (flu)*. Retrieved 03-13-2007 from <http://www.cdc.gov/flu>)

The **Ebola** virus causes Ebola hemorrhagic fever, an often fatal disease that affects humans and primates. Much is unknown about this virus, but it is believed to originate from an animal host that is native to the African continent. There is currently no treatment for infection. The Ebola virus is transmitted by direct contact with the blood, body fluids and tissues of infected persons. (CDC. *Questions and answers about Ebola hemorrhagic fever*. Retrieved 03-13-2007 from <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/ebola/qa.htm>: World Health Organization. Retrieved 7-11-2007 from <http://www.who.int/csr/disease/ebola/en/>)

The **Omsk** virus is transmitted through an infected tick bite and causes neurological diseases and haemorrhagic fever. (Charrel, R. N., Attoui, H., Butenko, A. M., Clegg, J. C., Deubel, V., Frolova, T. V., Gould, E. A., Gritsun, T. S., Heinz, F. X., Labuda, M., Lashkevich, V. A., Loktev, V., Lundkvist, A., Lvov, D. V., Mandl, C. W., Niedrig, M., Papa, A., Petrov, V. S., Plyusnin, A., Randolph, S., Suss, J., Zlobin, V. I., & de Lamballerie, X. (2004) Tick-borne virus diseases of human interest in Europe. *Clinical Microbiology Infection*, 10(12), 1040-1055.)

The **Junin** virus (in the same family as the *Lassa* virus, arenavirus) causes Argentine hemorrhagic fever. Viruses in this family usually are associated with a specific rodent species. (Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/arena.htm>)

A rabies-like virus, **Duvenhage** virus, is associated with bats in Africa and leads to rabies-like disease in humans. (*Duvenhage virus*. Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/eid/vol12no12/06-0764.htm>)

The **Oropouche** virus is an important arthropod-borne virus that infects humans and causes Oropouche fever. It is a health threat in subtropical areas of South and Central America. (Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/eid/vol11no10/05-0464.htm>)

The **Orf** virus that infects humans is associated with sheep, goats and other small ruminants. Orf causes ulcerative lesions in infected individuals. (Retrieved 03-19-2007 from <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5503a1.htm>)

The **Coxsackievirus** causes hand-foot-and-mouth disease, typically in young children. It is a mild disease that appears as a rash with very small blisters on the skin. (U.S. National Library of Medicine. *Hand-foot-mouth disease*. NIH. Retrieved 03-13-2007 from <http://www.nlm.nih.gov/medlineplus/ency/article/000965.htm>)

A rare viral fever, **Chikungunya**, is spread by mosquitoes to humans. Disease symptoms include fever, headache, nausea, and muscle and joint pain. (Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/dvbid/Chikungunya/chikvfact.htm>)

Bunyamwera viruses are associated with congenital defects in humans. (Retrieved 03-19-2007 from <http://www.cdc.gov/ncidod/eid/vol11no4/calishr3.htm>)



Herpes: Herpes simplex virus (HSV) has two forms: Type I, which generally causes fever blisters and cold sores in the mouth and on the lips; Type II, which is associated with the genital area, but can infect the mouth. (Retrieved 03-19-2007 from <http://www.niaid.nih.gov/factsheets/stdherp.htm>)

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Image Reference

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<h2 style="text-align: center;">Virus – Human Herpes</h2> <hr/> <ul style="list-style-type: none"> ■ Shape: <ul style="list-style-type: none"> ■ Electron microscope images reveal an Icosahedral pattern (20 faces of equilateral triangles) ■ Genetic information: <ul style="list-style-type: none"> ■ double-stranded DNA ■ Infection: <ul style="list-style-type: none"> ■ Can persist in the host and be reactivated ■ Eight of the known herpes viruses infect humans 	 <p>Icosahedron 20 Triangles</p>
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Transcript from “Viruses,” National Center for Macromolecular Imaging

Looking closely at one of them, human herpes virus reveals a lot about how all viruses work. With an advanced electron microscope, researchers can see this relatively large and complex virus as acutely as a CAT scan sees the body in three dimensions. There are more than one hundred herpes viruses, eight that infect humans.

Additional information:

Electron microscope images have helped us understand the shape of the Human Herpes Virus. The shape of a herpes virus is an icosahedron (20 triangular faces).

References

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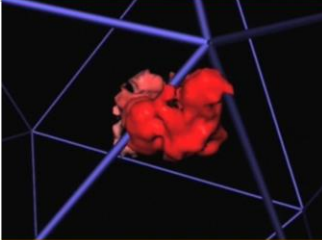
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Herpes – Etymology and History

- From Greek, meaning to creep
- Hippocrates noted Herpes lesions (460 - 370 B.C.)
- Oral Herpes lesions also are known as “fever blisters,” and “cold sores”



Herpes virus 1
Viral Protein 5



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From the Greek, "herpes" means to creep, to crawl. Hippocrates, who founded modern medical practice, noted the creeping lesions in his records thousands of years ago. Most people have herpes virus and don't know it. Chicken pox, which is human herpes virus 3, infects 97 percent of Americans. It can recur later in life, and it's called shingles. Mononucleosis is caused by human herpes virus 4. Cold sores are caused by herpes viruses 1 and 2. More than 80 percent of Americans have herpes virus 1, and somewhere between 20 percent to 60 percent of Americans have herpes virus 2. The human herpes viruses are transmitted by touching, kissing, sex, and bodily fluids - none is airborne.

Additional information:

Shown is a view of computationally isolated Viral Protein 5 of Herpes Simplex Type 1 Virion.

Reference

Dougherty, M. & Chiu, W. (1996). *Viruses*. National Center for Macromolecular Imaging.

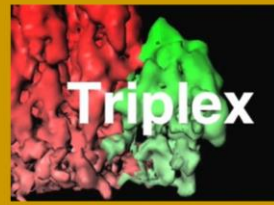
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Image Reference

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Herpes Virus Type 1 – Structure

- Four compartments can be visualized using an electron microscope
 - Envelope: Outer lipid bilayer
 - Tegument: Middle layer
 - Capsid: Inner most layer
 - Core: double stranded DNA
- Capsid is an icosahedron with 12 pentons and 150 hexons:
 - There are five copies of VP5 (viral protein five) in a penton and six copies in a hexon.
 - Pentons and hexons are surrounded and connected by triplexes



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Transcript from “Viruses,” National Center for Macromolecular Imaging

With the electron microscope, the four parts of the cold sore virus, herpes virus 1, are visible. When it has a chance to invade a healthy cell, the virus behaves like the Trojan horse. Its sticky outer shell of proteins, fats and sugars tricks the cell so the cell absorbs the virus. But once inside, the virus breaks apart and its genetic poison attacks the cell's nucleus. The virus's DNA reprograms the cell's DNA. The cell's new job is to make hundreds of thousands of copies of the virus. When its work is done, the cell dies.

Additional Virus information:

Triplex, Penton and Hexon all are structural units of the capsid. The capsid of the Herpes Virus type virion is an icosohedron made of 12 pentons and 150 hexons that are surrounded and connected by triplexes.

References

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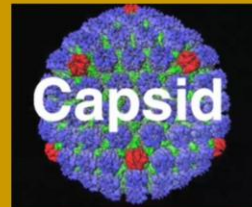
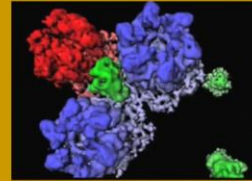
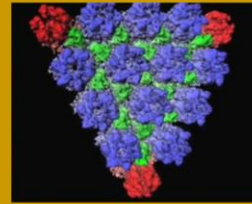
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Image Reference

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Viruses – Disease

- Viral infections generally behave in two ways:
 - Viruses reproduce and cause disease immediately (active or lytic).
 - Viruses integrate into the host cell (dormant or latent).



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Sometimes the virus takes a different path. Instead of reproducing, it will hide in the cell's DNA, waiting, often decades, to begin its takeover. This is why you can have chicken pox at six and shingles at 60. Acyclovir was one of the first antiviral agents, and it's prescribed to combat human herpes viruses 1, 2 and 3. Like smallpox, herpes will become a disease of the past. Directed by the National Institutes of Health, medical researchers aggressively work to understand and control the biochemistry of viruses. They know pursuing and eradicating them will end much disease and human suffering.

Additional information:

A capsid is the protein shell that protects the genome of the virus.

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Image Reference

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Viruses

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Reference

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