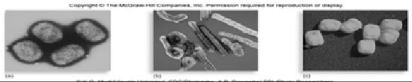
Lecture 5 (Ch6) - Viruses

- Topics
  - Characteristics
  - Structure/Classification
  - Multiplication
  - Cultivation and replication
  - Non-viral infectious agents
  - Treatment



1

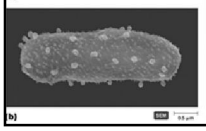
Virus Characteristics

- obligate intracellular parasites
- not cells
- tiny! - 20nm -450nm (no light scope)
- do not independently fulfill characteristics of life
- active only inside the cell
- surface molecules confer high specificity
- use hosts genetic material
- lack enzymes or machinery for synthesis

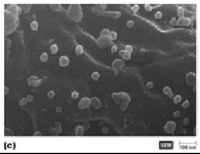
2

Viral Host Range

(a)



(b)



(c)

Most infect only specific host (attachment)
Can be so specific only infect specific type of cell in specific host
Some generalists – infect many kinds of cells in many different hosts

3

Structure

- Size and morphology
- Capsid
- Envelope
- Complex
- Nucleic acid

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Virus- inside & out

- **Extracellular**
  - Called virion
  - Protein coat (capsid) surrounding nucleic acid
  - Nucleic acid and capsid also called nucleocapsid
  - Some have phospholipid envelope
  - Outermost layer provides protection and recognition sites for host cells
- **Intracellular**
  - Capsid removed
  - Virus exists as nucleic acid

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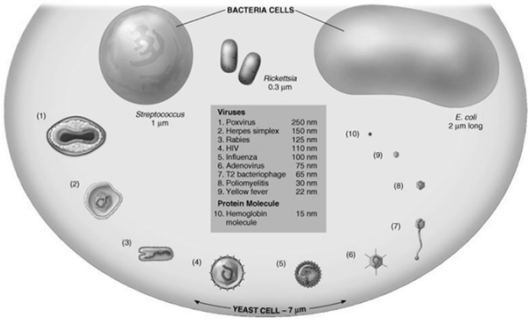
Size Comparison



Size comparison of viruses

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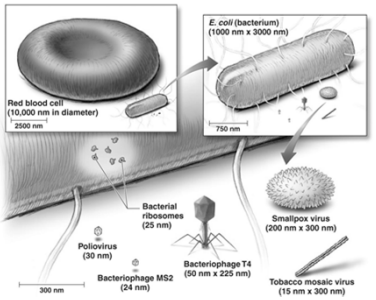
More Size…



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Looking at Virus

Electron microscopy, "negative" staining, positive staining, and shadow casting are methods of viewing viruses.

E.M. methods of viewing viruses

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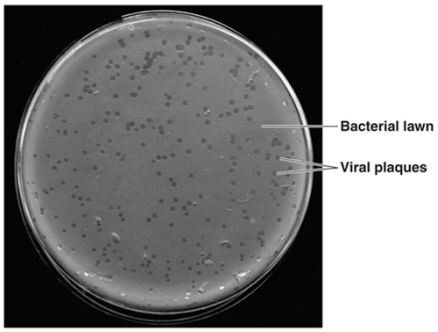
Visualizing Virus Indirectly



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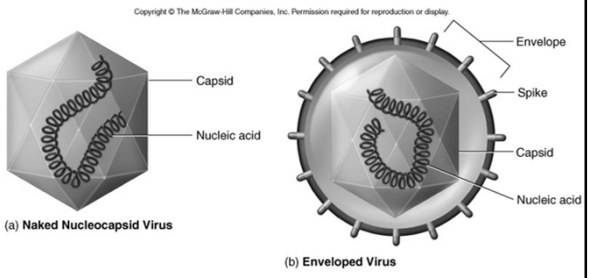
The two major structure types for viruses:

naked nucleocapsid virus

enveloped virus



Generalized viral structures

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Capsid

- Protective outer shell that surrounds viral nucleic acid
- Capsid spikes
- Composed of capsomer subunits
- Two types of capsids (based on shape):
  - Helical
  - Icosahedral

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Helical capsid

- Naked helical virus
  - Nucleocapsid is rigid and tightly wound into a cylinder-shaped package
  - Example: Tobacco mosaic virus
- Enveloped helical virus
  - Nucleocapsid is more flexible than naked virus
  - Examples: Influenza, measles, rabies

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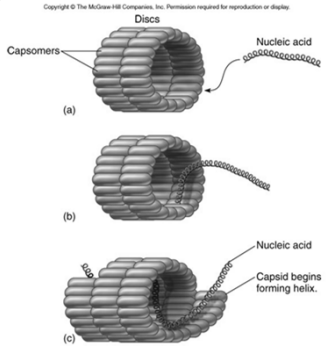
Helical capsids:
rod-shaped capsomers form hollow discs, like a bracelet.



Helical nucleocapsid assembly

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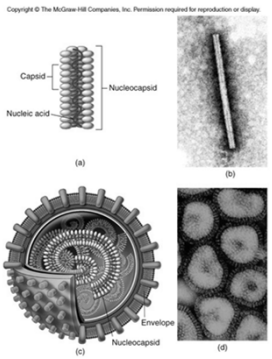
Comparison: naked helical plant virus and an enveloped helical human virus.



Typical variation of viruses with helical Nucleocapsids.

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Icosahedron capsid

- Three-dimensional, 20-sided with 12 evenly spaced corners
- Variation in capsomer number
  - Polio virus 32 capsomers
  - Adenovirus 240 capsomers

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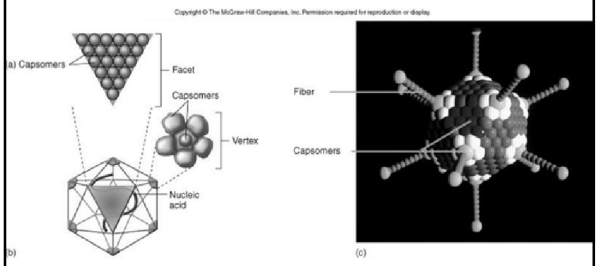
The structure and formation of an adenovirus



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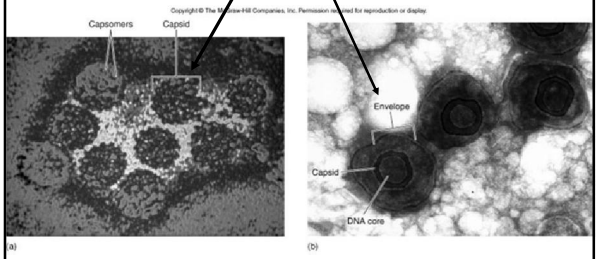
Icosahedral viruses –
can be naked or enveloped.



Two types of icosahedral viruses

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Viral Envelope

- Lipid and proteins
- Envelope spikes
- During release of animal viruses, a part of the host membrane is taken
- Enable pleomorphic shape of the virus
  - Spherical
  - Filamentous
- Recognition & Attachment

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Function of the capsid/envelope

- Protect nucleic acid from the host's acid- and protein-digesting enzymes
- Assist in binding and penetrating host cell
- Stimulate the host's immune system

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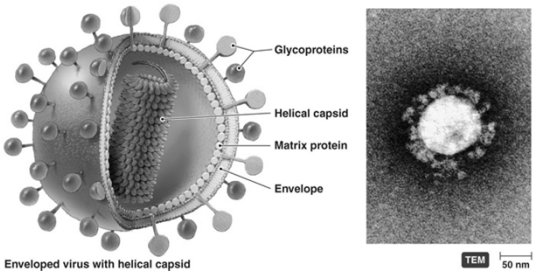
An Enveloped Virus



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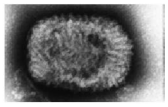
Complex viruses

- Structure is more intricate than helical or icosahedral viruses. Examples:
  - Pox virus
    - Several layers of lipoproteins
    - Course surface fibrils
  - Bacteriophage (next slide)
    - Polyhedral head
    - Helical tail
    - Fibers for attachment



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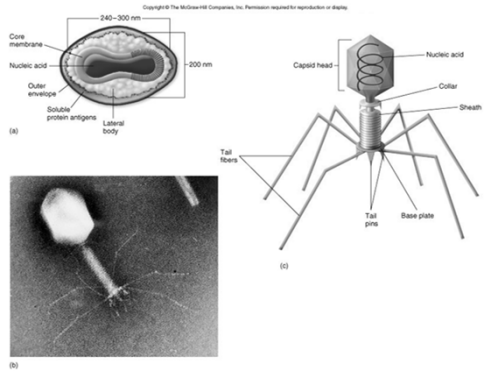
Pox virus and T4 bacteriophage



Detailed structure of complex viruses

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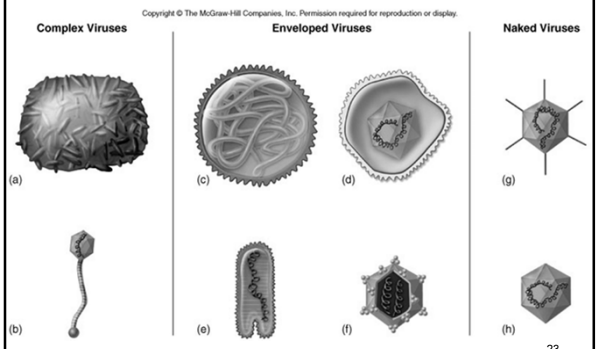
Morphology: (helical, icosahedral, complex) of a naked virus, enveloped virus and a complex virus.



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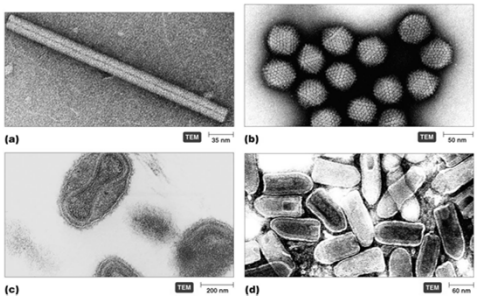
Virion Shapes in EM



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Viral nucleic acid

- Viruses contain either DNA or RNA
- Possess only the genes to invade and regulate the metabolic activity of host cells
  - Examples:
    Hepatitis B (DNA)(4 genes)
    Herpesviruses (DNA) (100 genes)
    Rotavirus (dsRNA)
    Coronavirus, SARs (ssRNA)
- No viral metabolic genes, because uses host's metabolic resources

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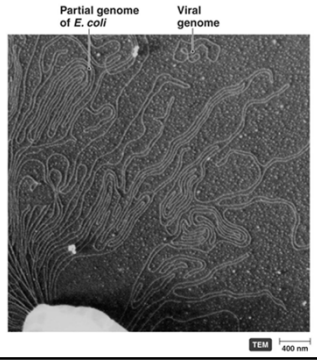
Compare Genome Size



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The 7 classes of virus

- DNA viruses contain classes I, II, and VII
- RNA viruses contain classes III-VI.

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DNA virus classes (I, II, VII)

- Class I viruses:
  - double-stranded DNA (dsDNA) genome
  - Examples:
    - Some phages
    - Family *Herpesviridae (*includes human herpesviruses), *Varicella Zoster*, *Poxviridae*, JC, *papilloma*
- Class II viruses:
  - +sense single-stranded DNA (ssDNA) genome.
  - Example: *Parvoviridae*
- Class VII viruses:
  - double-stranded, reverse transcriptase (dsDNA-RT) genome.
  - Example: *Hepadenovirus*

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RNA virus classes (III-VI)

- Class III viruses:
  - double-stranded RNA (dsRNA) genome.
  - Example: *Reovirus*
- Class IV viruses:
  - +sense single-stranded RNA (ssRNA) genome (acts as mRNA). Example: *Picornaviruses*,
- Class V viruses:
  - -sense single-stranded RNA (ssRNA) genome used as a template for mRNA synthesis.
  - Example: *Rhabdovirus*
- Class VI viruses:
  - +sense single- stranded reverse transcriptase RNA (ssRNA-RT) genome (with DNA intermediate in replication and also mRNA synthesis).
  - Example: *Retroviridae*

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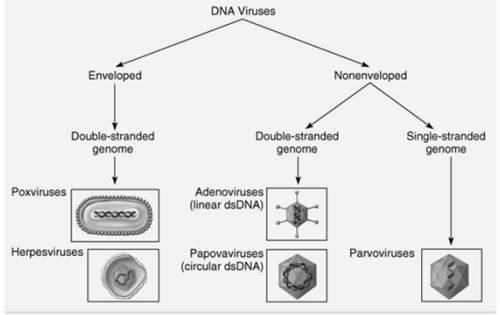
Examples of medically important DNA viruses

TABLE 6.2 Medically Relevant DNA Virus Groups



Adapted from: *Poxviridae* from Buller et al., National Institute of Allergy & Infectious Disease, Department of Health & Human Services.

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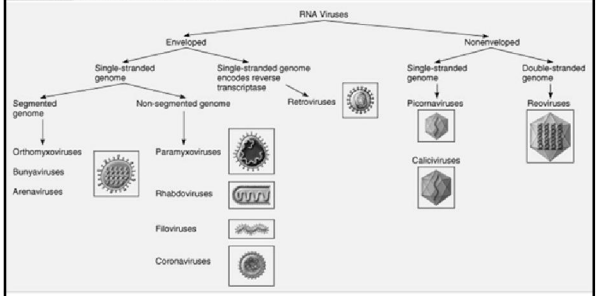
Some medically important RNA viruses

TABLE 6.3 Medically Relevant RNA Viruses



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Virus & Cancer

- Animal's genes dictate some cells can no longer divide and those that can divide are prevented from unlimited division
- Genes for cell division "turned off" or genes inhibiting division "turned on"
- Neoplasia
  - Uncontrolled cell division in multicellular animal; mass of neoplastic cells is tumor
- Benign vs. malignant tumors
  - Metastasis
  - Cancers

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Oncogene Theory

(induction of cancer in humans)

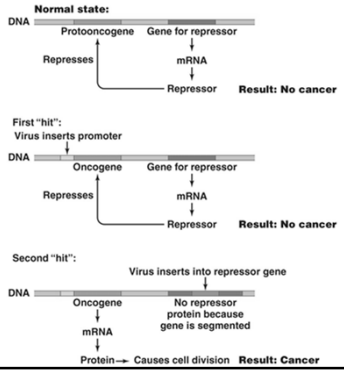

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Figure 13.16

Environmental Factors, Viruses &Cancer

- Environmental factors that contribute to the activation of oncogenes
  - Ultraviolet light
  - Radiation
  - Carcinogens
  - Viruses

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Virus & Cancer

- Viruses cause **20–25%** of human cancers
  - Some carry copies of oncogenes as part of their genomes
  - Some promote oncogenes already present in host
  - Some interfere with tumor repression when inserted into host's repressor gene
- Specific viruses are known to cause ~15% of human cancers
  - Burkitt's lymphoma
  - Hodgkin's disease
  - Kaposi's sarcoma
  - Cervical cancer

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Classification

- Structure
- Chemical composition
- Genetic makeup
- Host relationship
- Type of disease

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Three orders of viruses developed for classification.

TABLE 6.4 Examples from the Three Orders of Viruses

Genome Type	Order	Family	Genus	Species
dsDNA	Caudovirales	Poxviridae	Orthopoxvirus	Vaccinia virus
neg (ss)RNA	Mononegavirales	Paramyxoviridae	Morbillivirus	Measles virus
pos (ss)RNA	Nidovirales	Togaviridae	Rubivirus	Rubella virus

Adapted from van Regenmortel, M., editor, et al. 2000. *Virus Taxonomy. Seventh Report of the International Committee on Taxonomy of Viruses.* New York: Academic Press.

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Classification of important human viruses

TABLE 6.5 Important Human Virus Families, Genera, Common Names, and Types of Diseases

	Family	Genus of Virus	Common Name of Genus Members	Name of Disease
DNA Viruses	Poxviridae	*Orthopoxvirus*	Variola and vaccinia	Smallpox, cowpox
	Herpesviridae	*Simplexvirus*	Herpes simplex (HSV-1) virus	fever blister, cold sores
			Herpes simplex (HSV-2) virus	Genital herpes
		Varicellovirus	Varicella-zoster virus (VZV)	Chickenpox, shingles
		Cytomegalovirus	Human cytomegalovirus (CMV)	CMV infections
	Adenoviridae	*Mastadenovirus*	Human adenoviruses	Adenovirus infection
	Papovaviridae	*Papillomavirus*	Human papillomavirus (HPV)	Several types of warts
		Polyomavirus	JC virus (JCV)	Progressive multifocal leukoencephalopathy (PML)
	Hepadnaviridae	*Hepadnavirus*	Hepatitis B virus (HBV or Dane particle)	Serum hepatitis
	Parvoviridae	*Erythrovirus*	Parvovirus B19	Erythema infectiosum

RNA Viruses	Picornaviridae	*Enterovirus*	Poliovirus	Poliomyelitis
			Coxsackievirus	Hand-foot-mouth disease
		Hepatovirus	Hepatitis A virus (HAV)	Short-term hepatitis
		Rhinovirus	Rhinovirus	Common cold, bronchitis
	Caliciviridae	*Calicivirus*	Norwalk virus	Viral diarrhea, Norwalk virus syndrome
	Togaviridae	*Alphavirus*	Eastern equine encephalitis virus	Eastern equine encephalitis (EEE)
			Western equine encephalitis virus	Western equine encephalitis (WEE)
			Yellow fever virus	Yellow fever
			St. Louis encephalitis virus	St. Louis encephalitis
		Rubivirus	Rubella virus	Rubella (German measles)
	Flaviviridae	*Flavivirus*	Dengue fever virus	Dengue fever
			West Nile fever virus	West Nile fever
	Bunyaviridae	*Bunyavirus*	Bunyamwera viruses	California encephalitis
		Hantavirus	Sin Nombre virus	Respiratory distress syndrome
		Phlebovirus	Rift Valley fever virus	Rift Valley fever
		Nairovirus	Crimean-Congo hemorrhagic fever virus (CCHF)	Crimean-Congo hemorrhagic fever
	Filoviridae	*Filovirus*	Ebola, Marburg virus	Ebola fever
	Reoviridae	*Coltivirus*	Colorado tick fever virus	Colorado tick fever
		Rotavirus	Human rotavirus	Rotavirus gastroenteritis
	Orthomyxoviridae	*Influenza virus*	Influenza virus, type A (Asian, Hong Kong, and swine influenza viruses)	Influenza or "flu"
	Paramyxoviridae	*Paramyxovirus*	Parainfluenza virus, types 1–3	Parainfluenza
			Mumps virus	Mumps
		Morbillivirus	Measles virus	Measles (red)
		Pneumovirus	Respiratory syncytial virus (RSV)	Common cold syndrome
	Rhabdoviridae	*Lyssavirus*	Rabies virus	Rabies (hydrophobia)
	Retroviridae	*Oncovirinae*	Human T-cell leukemia virus (HTLV)	T-cell leukemia
		Lentivirus	Human immunodeficiency virus 1 and 2	Acquired immunodeficiency syndrome (AIDS)
	Arteriviridae	*Arterivirus*	Lassa virus	Lassa fever
	Coronaviridae	*Coronavirus*	Infectious bronchitis virus (IBV)	Bronchitis
			Enteric corona virus	Coronavirus enteritis
			SARS virus	Severe acute respiratory syndrome

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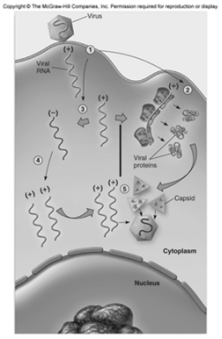
Replication/Multiplication

- Adsorption
- Penetration
- Uncoating
- Synthesis
- Assembly
- Release



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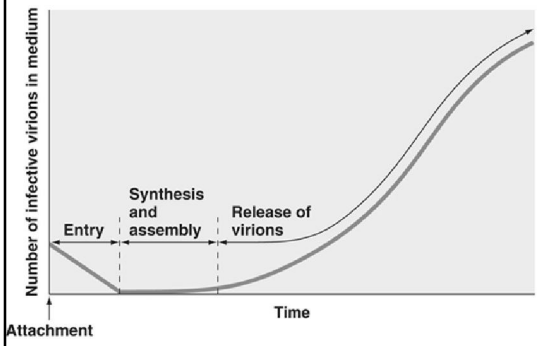
Virions in Persistent Infection



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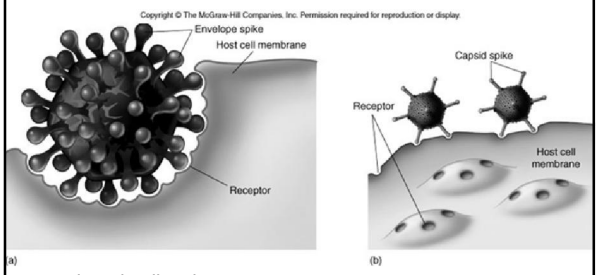
Adsorption to Host Cell



enveloped spike virus

naked capsid spike virus.

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Penetration of animal viruses occur by endocytosis or fusion between the viral envelope and the host cell membrane

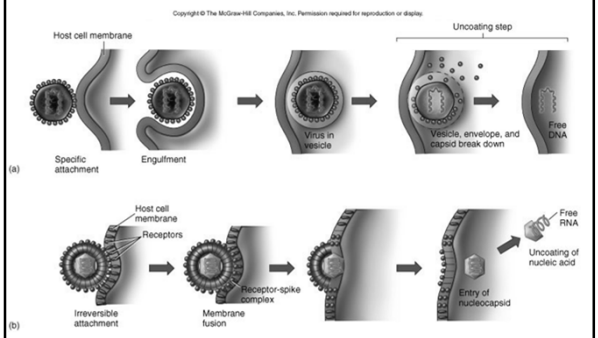

Fig. 6.13 Two principal means by which animal viruses penetrate.

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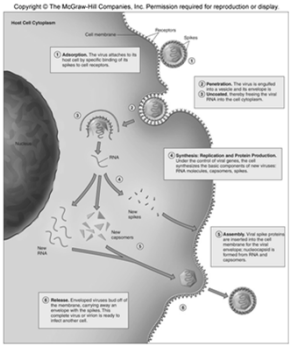
Uncoating and synthesis of viruses rely on the host's metabolic systems.



Multiplication cycle general features of enveloped animal virus.

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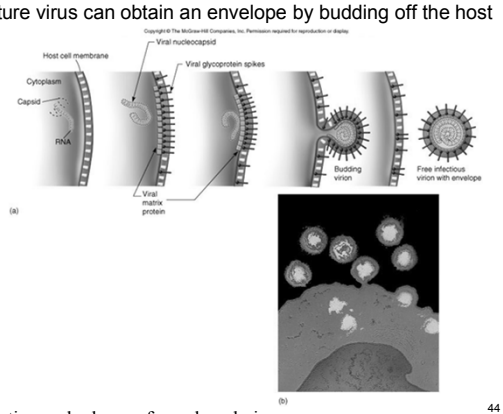
A mature virus can obtain an envelope by budding off the host cell.



Maturation and release of enveloped viruses

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Cytopathic effects

- Damage to the host cell due to a viral infection
  - Inclusion bodies
  - Syncytia
  - Chronic latent state
  - Transformation

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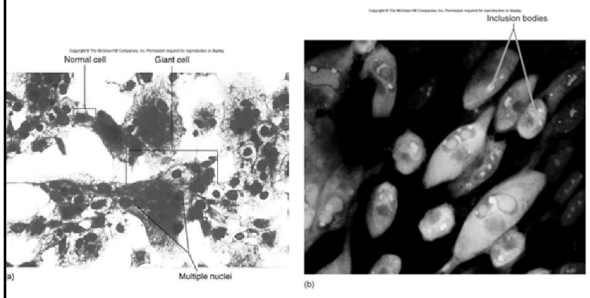
Syncytia and inclusion bodies



Cytopathic changes in cells and cell cultures infected by viruses

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Bacteriophage

- Bacterial virus
- Multiplication is similar to animal viruses except for the penetration (inject DNA), release (lyses) and prophage (lysogeny) stages
- Useful as alternate therapy

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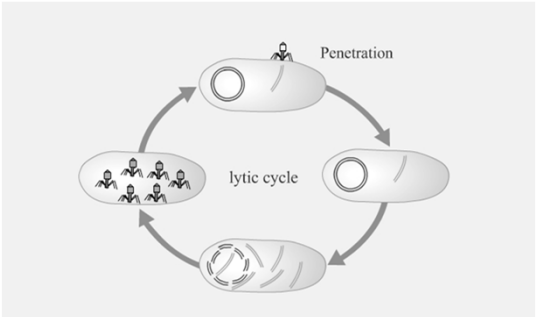
Lytic Cycle



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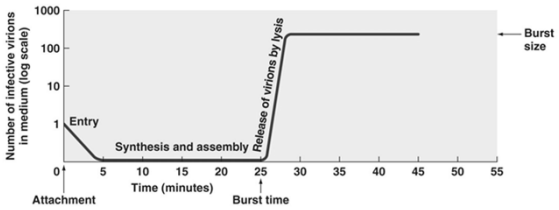
Viral Lytic Cycle



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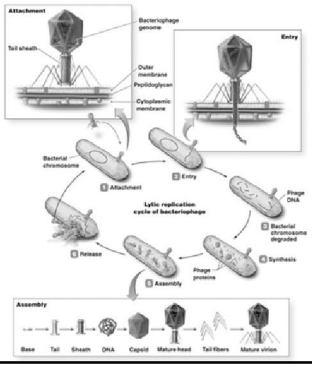
Viral Lytic Cycle



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Lysogeny

- Modified replication cycle
- Infected host cells grow and reproduce normally for generations before they lyse
- Temperate phages
  - Prophages – inactive phages
- Lysogenic conversion results when phages carry genes that alter phenotype of a bacterium

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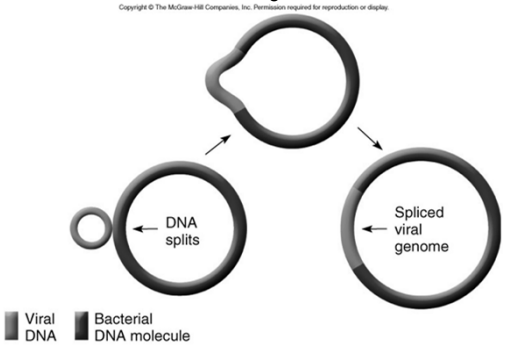
Lysogeny is when the bacteriophage inserts its DNA into the bacterial host genome.



The lysogenic state in bacteria

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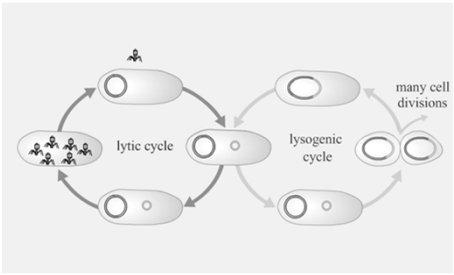
Lytic to Lysogenic



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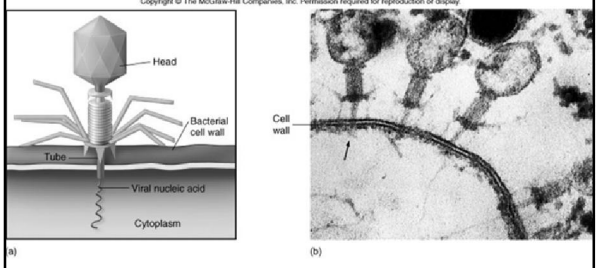
T-even bacteriophage penetrate the host cell by specifically binding and injecting their DNA into the host cell.



Penetration of a bacterial cell by a T-even bacteriophage.

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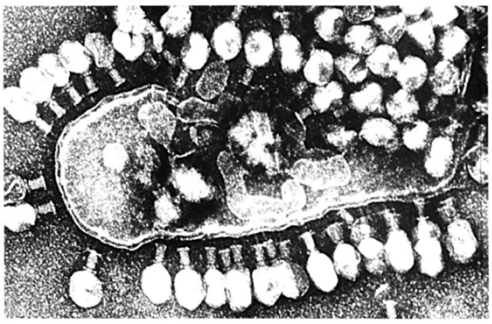
After viral multiplication inside the host cell, viral enzymes weaken the host cell membrane, lyse the cell, and release virions



A weakened bacterial cell, crowded with viruses.

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Comparison: bacteriophage and animal virus multiplication

TABLE 6.7 Comparison of Bacteriophage and Animal Virus Multiplication

	Bacteriophage	Animal Virus
Adsorption	Precise attachment of special tail fibers to cell wall	Attachment of capsid or envelope to cell surface receptors
Penetration	Injection of nucleic acid through cell wall; no uncoating of nucleic acid	Whole virus is engulfed and uncoated, or virus surface fuses with cell membrane, nucleic acid is released
Synthesis and Assembly	Occurs in cytoplasm Cessation of host synthesis Viral DNA or RNA is replicated and begins to function Viral components synthesized	Occurs in cytoplasm and nucleus Cessation of host synthesis Viral DNA or RNA is replicated and begins to function Viral components synthesized
Viral Persistence	Lysogeny	Latency, chronic infection, cancer
Release from Host Cell	Cell lyses when viral enzymes weaken it	Some cells lyse; enveloped viruses bud off host cell membrane
Cell Destruction	Immediate	Immediate or delayed

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Cultivation and Replication

- *In vivo* methods
  - Laboratory animals
  - Embryonic bird tissues
- *In vitro* methods
  - Cell or tissue culture

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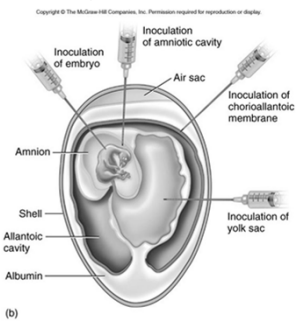
Early developing bird embryos have a protective case that provides an ideal viral propagation environment



Cultivating animal viruses in a developing bird embryo

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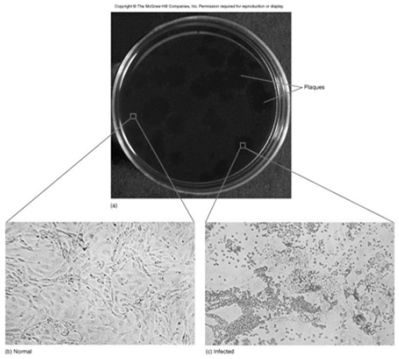
A monolayer of monkey kidney cells is a cell culture that enables virus propagation



Normal and infected cell cultures

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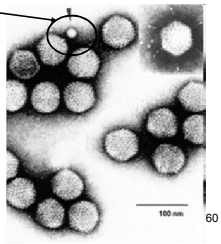
Non-cellular Infectious Agents

- Prions (naked proteins)
- Satellite viruses (usually plant virus associated for purpose of replication)
- Viroids (unique plant pathogens, small, single-stranded, circular RNA)



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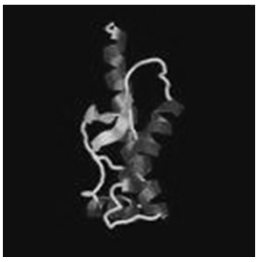
Prions

- Protein particle with no nucleic acid, no envelope, no capsid
- Diseases
  - *Creutzfeldt-Jakob*
  - "mad cow disease"



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Prion Diseases

- Fatal neurological degeneration, fibril deposits in brain, and loss of brain matter
- Large vacuoles form in brain
  - Characteristic spongy appearance
- Spongiform encephalopathies – BSE, vCJD, kuru
- Prions only destroyed by incineration or autoclaving in 1 N NaOH

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Prions (cont…)

- Cellular PrP protein
  - Made by all mammals
  - Normal structure with α-helices called cellular PrP
- Prion PrP
  - Disease-causing form with β-sheets called prion PrP
- Prion PrP converts cellular PrP into prion PrP by inducing conformational change

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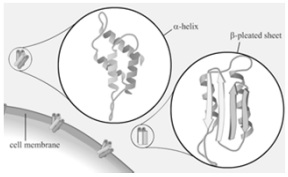
Prion Protein Folding

- Normally, nearby proteins and polysaccharides force PrP into cellular shape
- Excess PrP or PrP mutations result in formation of prion PrP
  - Cause newly synthesized cellular PrP to refold into prion PrP



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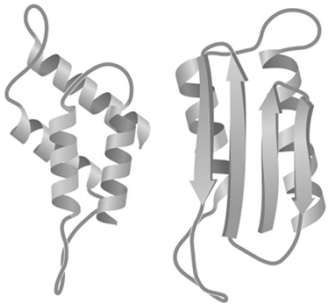
Stable Prion Protein (PrP) Forms



(a) Cellular PrP (b) Prion PrP

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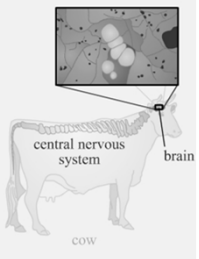
The Prion Diseases

human prion diseases	animal prion diseases
Creutzfeldt-Jakob disease	scrapie
Gerstmann-Straussler-Scheinker syndrome	transmissable mink encephalopathy
fatal familial insomnia	chronic wasting disease
kuru	bovine spongiform encephalopathy ("mad cow disease")



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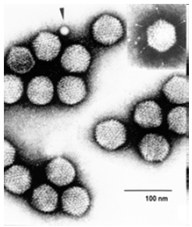
Satellite viruses

- Dependent on other viruses for replication
- Ex. Delta agent, which is only expressed in the presence of hepatitis B virus, depend on it for replication- the only viroid like infectious agent of animals.



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Viroids

- Plant pathogens
  - Tomatoes, potatoes, cucumbers.
- 1/10th the size of normal viruses
- Naked strands of RNA, no capsid

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Example Viroid Effects

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