

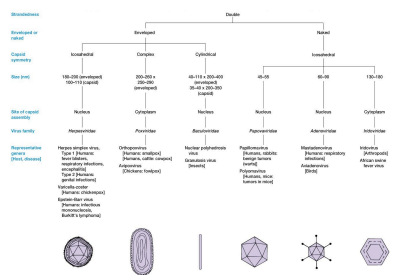
Chapter 18

The Viruses: Viruses of Eucaryotes

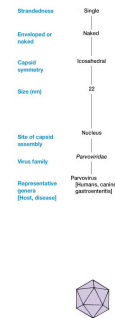
Classification of Animal Viruses

- most important criteria
 - morphology
 - nucleic acid properties
 - genetic relatedness
 - determined by numerous techniques, including sequencing data and nucleic acid hybridization

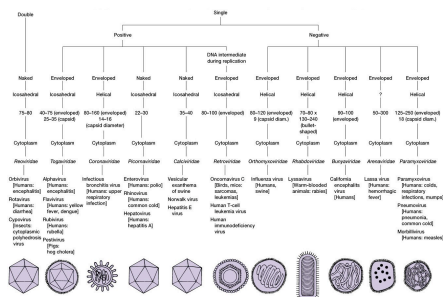
Double-stranded DNA viruses



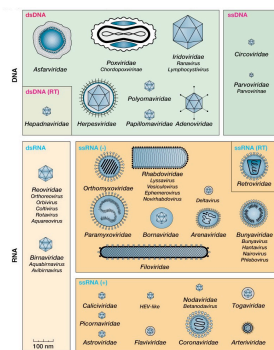
Single-stranded DNA viruses



RNA viruses



Major vertebrate-infecting viruses



Reproduction of Animal Viruses

- similar to reproduction of bacteriophages
 - adsorption
 - penetration and uncoating
 - replication of virus nucleic acids
 - synthesis and assembly of virions
 - release

Adsorption of Virions

- viral surface proteins and/or enzymes mediate attachment to specific host receptors

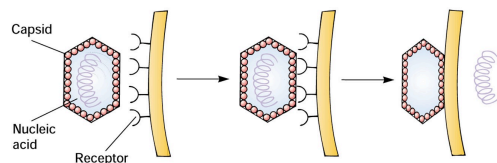
Table 18.1 Examples of Host Cell Surface Proteins That Serve as Virus Receptors

Virus	Cell Surface Protein
Adenovirus	Coxsackie adenovirus receptor (CAR) protein
Hepatitis B virus	Receptor for the CD81 complement protein on human B lymphocytes
Hepatitis A virus	Alpha 2-macroglobulin
Herpes simplex virus, type 1	Fibroblast growth factor receptor; a member of the tumor necrosis factor/nerve growth factor receptor family
Human immunodeficiency virus	CD4 protein on T helper cells, macrophages, and monocytes; CXCR-4 or the CCR5 receptor
Influenza A virus	Sialic acid-containing glycoprotein
Mumps virus	CD46 complement regulator protein
Poliovirus	Immunoglobulin superfamily
Rabies virus	Acetylcholine receptor on neurons
Rhinovirus	Intercellular adhesion molecules (ICAMs) on the surface of respiratory epithelial cells
Rotavirus, type 3	β -adrenergic receptor
Rotavirus	Acetylated sialic acid on glycoprotein
Vaccinia virus	Epidermal growth factor receptor

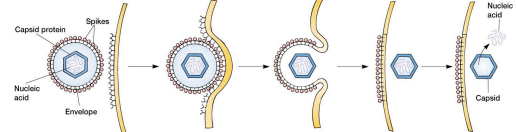
Penetration and Uncoating

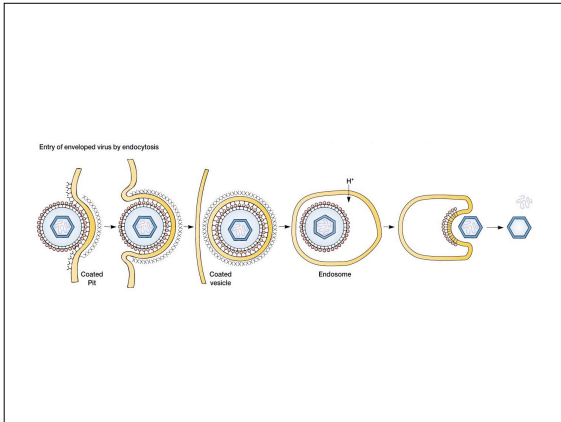
- three mechanisms
 - injection of nucleic acid
 - fusion of envelope with host membrane
 - endocytosis

Direct penetration by naked viruses



Enveloped virus fusing with plasma membrane





Replication and Transcription in DNA Viruses

- early genes
 - encode proteins involved in take over of host and in synthesis of viral DNA and RNA
- viral DNA replication
 - usually occurs in nucleus
- early mRNA synthesis
 - usually by host RNA polymerase

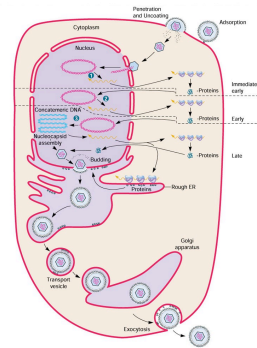
e.g., parvoviruses

- single-stranded DNA (ssDNA) viruses
- small genomes with overlapping genes
 - only encode capsid proteins
- use host enzymes for all biosynthetic processes
 - viral DNA only replicated during S period of cell cycle

e.g., herpes simplex virus I

uses host RNA polymerase for synthesis of viral mRNA

uses virus-encoded DNA polymerase for replication of genome



e.g., poxviruses

- large, morphologically complex double-stranded DNA (dsDNA) viruses
- virion carries DNA-dependent RNA polymerase that synthesizes early mRNA
 - encodes DNA polymerase and other enzymes needed for DNA replication

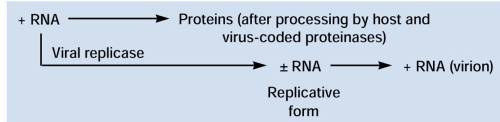
e.g., hepadnaviruses

- circular, dsDNA genome
- genome transcribed by host RNA polymerase
 - generates several mRNA molecules
 - one is large RNA (pregenome)
 - others encode polymerase with reverse transcriptase activity
- pregenome converted to dsDNA by virus polymerase

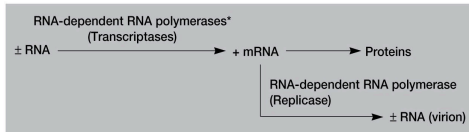
Replication and Transcription in RNA Viruses

- very diverse reproductive strategies
- four general modes of replication and transcription

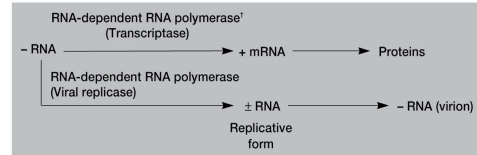
Positive single-stranded RNA viruses (picornaviruses)



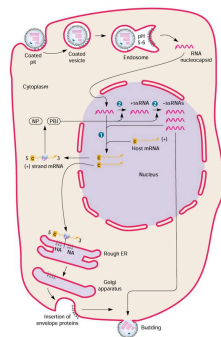
Double-stranded RNA viruses (reoviruses)



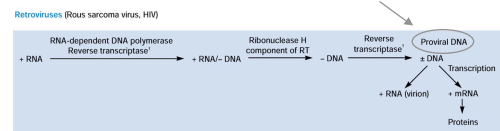
Negative single-stranded RNA viruses (paramyxoviruses—mumps and measles; orthomyxoviruses—influenza)



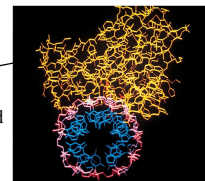
e.g., influenza virus



integrates into host chromosome



ribonuclease H complexed with DNA/RNA hybrid



RNA
DNA

Synthesis and Assembly of Virus Capsids

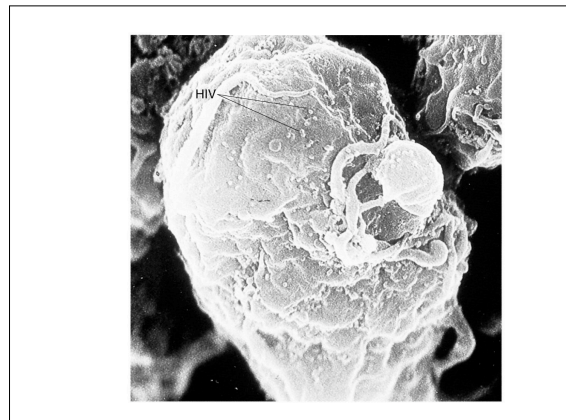
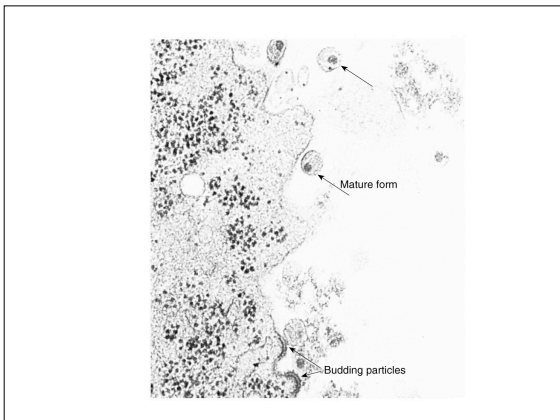
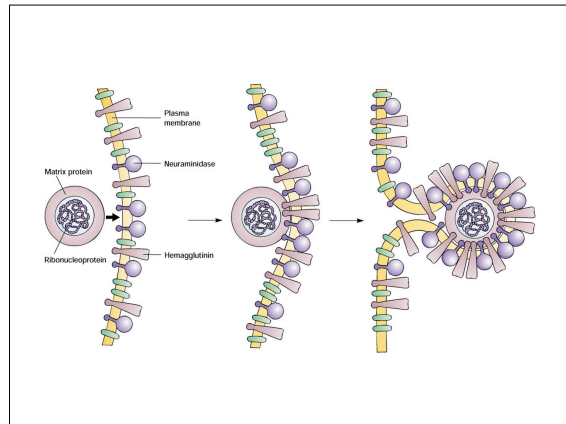
- capsid proteins
 - encoded by late genes
- assembly of naked viruses
 - empty procapsids formed then nucleic acid inserted
- assembly of envelope viruses
 - in most cases, similar to assembly of naked viruses
- site of morphogenesis varies

Table 18.2 Intracellular Sites of Animal Virus Reproduction

Virus	Nucleic Acid Replication	Capsid Assembly	Membrane Used in Budding
DNA Viruses			
Adenoviruses	Nucleus	Nucleus	
Hepadnaviruses	Cytoplasm	Cytoplasm	Endoplasmic reticulum
Herpesviruses	Nucleus	At nuclear membrane	Nucleus
Papillomaviruses	Nucleus	Nucleus	
Parvoviruses	Nucleus	Nucleus	
Polyomaviruses	Nucleus	Nucleus	
Poxviruses	Cytoplasm	Cytoplasm	
RNA Viruses			
Coronaviruses	Cytoplasm	Cytoplasm	Gold apparatus and endoplasmic reticulum
Orthomyxoviruses	Nucleus	Cytoplasm	Plasma membrane
Paramyxoviruses	Cytoplasm	Cytoplasm	Plasma membrane
Picornaviruses	Cytoplasm	Cytoplasm	
Rosaviruses	Cytoplasm	Cytoplasm	
Rotoviruses	Cytoplasm and nucleus	At plasma membrane	Plasma membrane
Rhabdoviruses	Cytoplasm	Cytoplasm	Plasma membrane, intracytoplasmic membranes
Togaviruses	Cytoplasm	Cytoplasm	Plasma membrane, intracytoplasmic membranes

Virion Release

- naked viruses
 - usually by lysis of host cell
- envelope viruses
 - formation of envelope and release usually occur concurrently
 - virus-encoded proteins incorporated into host membrane
 - nucleocapsid buds outward and is surrounded by modified host membrane



Virion release...

- envelope viruses...
 - for most, source of envelope is host plasma membrane

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DNA Viruses			
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Herpesviruses	Cytoplasm	Cytoplasm	Endoplasmic reticulum
Herpesviruses	Nucleus	At nuclear membrane	Nucleus
Papillomaviruses	Nucleus	Nucleus	
Parvoviruses	Nucleus	Nucleus	
Polioviruses	Nucleus	Nucleus	
Poxviruses	Cytoplasm	Cytoplasm	
RNA Viruses			
Coronaviruses	Cytoplasm	Cytoplasm	Golgi apparatus and endoplasmic reticulum
Orthomyxoviruses	Nucleus	Cytoplasm	Plasma membrane
Paramyxoviruses	Cytoplasm	Cytoplasm	Plasma membrane
Picornaviruses	Cytoplasm	Cytoplasm	
Retroviruses	Cytoplasm	Cytoplasm	
Retroviruses	Cytoplasm and nucleus	At plasma membrane	Plasma membrane
Rhabdoviruses	Cytoplasm	Cytoplasm	Plasma membrane, intracytoplasmic membranes
Togaviruses	Cytoplasm	Cytoplasm	Plasma membrane, intracytoplasmic membranes

Virion release...

- many viruses use host actin filaments to aid release process

Cytocidal Infections and Cell Damage

- cytocidal infection
 - infection that results in cell death

Mechanisms of host cell damage and cell death

- inhibition of host DNA, RNA, and protein synthesis
 - causes release of hydrolytic enzymes into cell
- alteration of plasma membrane
 - can lead to attack of host cell by immune system
 - can lead to cell fusion, forming syncytium

Other mechanisms...

- toxicity from high concentrations of viral proteins
- formation of inclusion bodies
 - can disrupt cell structure
- chromosomal disruptions
- transformation of host cell into malignant cell

Persistent, Latent, and Slow Virus Infections

- acute infections
 - rapid onset and relatively short duration
- persistent infections
 - can last many years

Types of persistent infections

- chronic virus infection
 - virus almost always detectable
 - clinical symptoms mild or absent for long periods
- latent infections
 - virus stops reproducing and remains dormant for some time
 - during latency, symptoms, antiviral-antibodies, and viruses are not detectable

Possible causes of persistent infections

- integration of viral genome into host genome
- decrease in antigenicity of virus
- mutation to less virulent and slower reproducing form
 - defective interfering (DI) particle – deletion mutant that cannot reproduce and slows reproduction of normal virus

Viruses and Cancer

- tumor
 - growth or lump of tissue
- neoplasia
 - abnormal new cell growth and reproduction due to loss of regulation
- anaplasia
 - reversion to a more primitive or less differentiated state
- metastasis
 - spread of cancerous cells throughout body

Carcinogenesis

- complex, multistep process
- often involves oncogenes
 - cancer-causing genes
 - many involved in regulation of cell growth and differentiation
- some viruses contribute to carcinogenesis

Viruses implicated in human cancers

Epstein-Barr virus	Burkitt's lymphoma nasopharyngeal carcinoma
Hepatitis B virus	liver cancer
Hepatitis C virus	liver cancer
Human herpesvirus 8	Kaposi's sarcoma
human papillomavirus	cervical cancer
HTLV-1 and HTLV-2	leukemia

Possible mechanisms by which viruses cause cancer

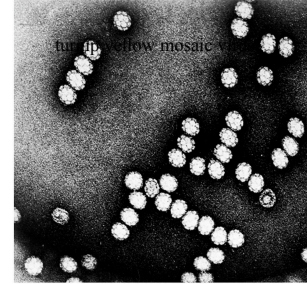
- carry oncogene into cell and insert it into host genome
- altered cell regulation due to changes in kinase activity or production of regulatory proteins
- insertion of promoter or enhancer next to cellular oncogene

Plant Viruses

- cause variety of plant diseases
- not as well studied as bacteriophages and animal viruses

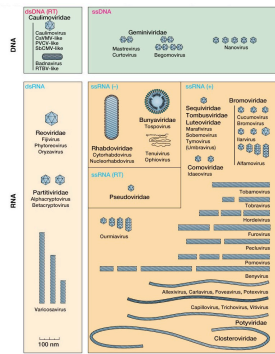
Virion Morphology

- does not differ significantly from that of animal or bacterial viruses



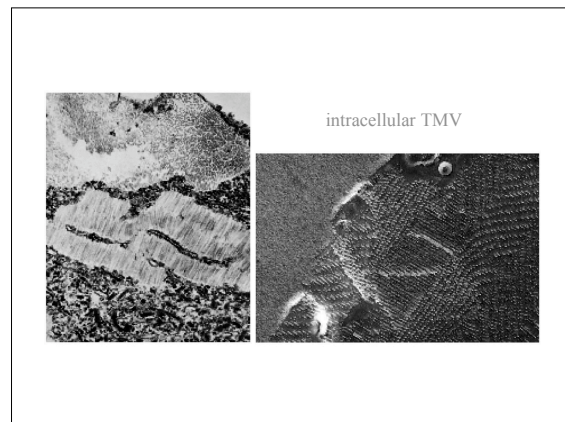
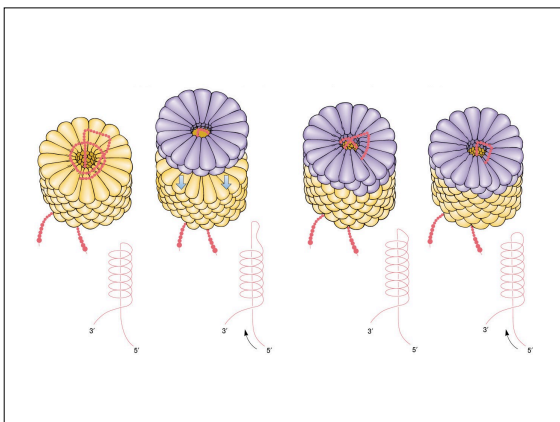
Plant Virus Taxonomy

- most are RNA viruses



Plant Virus Reproduction

- e.g., tobacco mosaic virus (TMV)
 - filamentous, plus strand RNA virus
 - RNA replication
 - unclear if catalyzed by host RNA-dependent RNA polymerase or virus encoded enzyme
 - protein synthesis
 - processed viral genome serves as mRNA
 - new virions assemble spontaneously



Transmission of Plant Viruses

- by wind, animals, seeds, tubers, and pollen
- usually requires mechanical damage to plant, due to tough plant cell walls
- insects that feed on plants most important agents of transmission

Viruses of Fungi and Algae

- fungal viruses
 - higher fungi
 - infected with dsRNA viruses
 - most cause latent infections
 - lower fungi
 - infected by dsRNA or dsDNA viruses
 - cause lysis
- algae
 - detected in electron micrographs, but not isolated

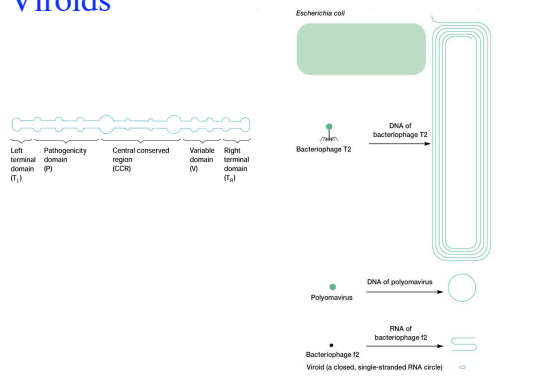
Insect Viruses

- belong to at least seven virus families
- infection often accompanied by formation of granular or polyhedral inclusion bodies
- have potential as biological control agents for insect pests

Viroids and Prions

- viroids
 - infectious agents composed only of circular ssRNA
- prions
 - infectious agent thought to be composed only of protein

Viroids



Viroids...

- do not act as mRNA molecules
- cause disease in plants
 - mechanism unknown
 - some cause latent infections
- RNA may be replicated by rolling-circle method using host RNA polymerase

Prions

- cause degenerative diseases in animals
 - e.g., scrapie
 - bovine spongiform encephalopathy
 - e.g., Creutzfeldt-Jakob disease
- currently thought that PrP (prion protein) is present in “normal” form in host animal
 - exposure to altered PrP thought to cause disease