Slide 1

Viruses

Lecture 16 and 17

Slide 2

Learning Outcomes

- Characteristics of Viruses
- Viral Taxonomy
- Viral Structure
- Viral Replication
- DNA viruses
- RNA viruses
- Prions

Slide 3

Characteristics of ALL Viruses

- 1. Viruses contain genetic material
  - Either DNA or RNA never both
- 2. Protein coat = Virion
- 3. Multiply inside living cells
- 4 Cause the synthesis of structures for their own transfer

Slide 4

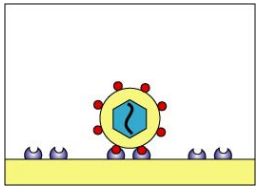
Viruses

- Are NOT composed of cells
- Do NOT belong in ANY of DOMAINS of Life
- Dependent upon host structures for replication
- ribosomes
- Pasteur
- 'Virus' derived from Greek root meaning poison
- Virulence derived from same root
- Measure of pathogenicity

Slide 5

Host Range of Viruses

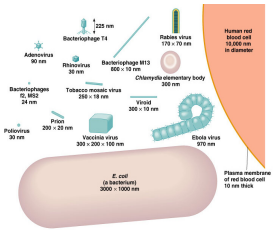
- Most viruses infect only specific types of cells in one host
- Host range is determined by specific host attachment receptors
- Polio
  - Narrow range
- Rabies
  - Broad host range



Slide 6

Relative Sizes

- Sizes measured in nm (1000 nm in 1 um)
- Small
- Picornaviruses
- Polio 30nm
- Large
- Vaccinia 300nm
- Overlap size of smallest bacteria
  - Chlamydia
  - Rickettsia



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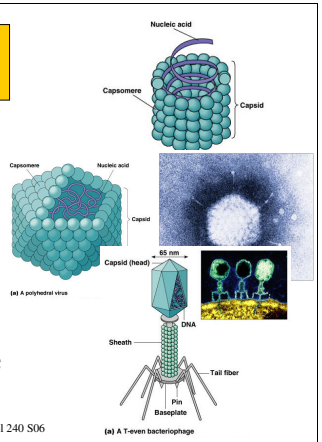
Virus Shapes

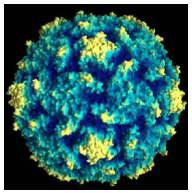
- Helical
- Polyhedral
- Enveloped
  - Spikes
  - glycoproteins
- Complex
  - bacteriophages
- All built from repeating protein units capsomeres



Slide 8

Viral Proteins

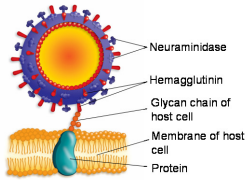
- 'Early Proteins'
- Enzymes
  - DNA or RNA Polymerases
  - protease
- 'Late Proteins'Structural Proteins
  - Capsid proteins
  - spikes
- Antigenicity due to difference in structural proteins
  - Serotypes
  - influenza
- Antibodies bind to structural proteins



Viral Envelope

- Components
  - Lipoprotein derived from host cell plasma membrane
  - Viral proteins
- Protein spikes
  - Attach to host cell receptors for hormones
  - Glycoproteins
  - Influenza
    - Hemagglutin
  - HIV
    - Gp 120
- Less resistant than non-enveloped viruses

Influenza A virus infects a host cell



Viral Taxonomy

- NOT included in any Domain of life
- Lack cells (cell theory)
- However named according to rules to name organisms

- Family names end in -viridae
- Genus names end in -virus

- Viral species: A group of viruses sharing the same genetic information and ecological niche (host). Common names are used for species
- Subspecies are designated by a number

Viral Taxonomy

- Herpesviridae
- Herpesvirus
- Human herpes virus 1
- HHV 2,
- HHV 3

- Retroviridae
- Lentivirus
- Human Immunodeficiency Virus 1, HIV 2

Herpes Viruses

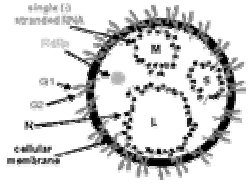
- Greek word *herpein* ("to creep")
- Many infections both latent and recurring
- HHV-1, HHV-2 - Herpes Simplex Viruses
  - Cold sores, genital herpes
- HHV-3 -Varicella-zoster
  - Chickenpox and shingles
- HHV-4 Epstein-Barr
  - Mononucleosis, Burkitt's Lymphoma
- HHV-5 - Cytomegalovirus
- HHV-6, HHV-7 - Roseolovirus
- HHV-8 Kaposi's Sarcoma

DNA Viruses

- Non-enveloped
- Adenoviridae
  - Mastadenovirus
  - Respiratory diseases
- Papillomaviridae
  - Papillomavirus
  - Warts
  - Polyomavirus
- Enveloped
- Herpesviridae
  - Simplexvirus (HHV-1 and 2)
  - Varicellovirus (HHV-3)
- Hepadnaviridae
  - Hep B
- Poxviridae
  - Pox viruses
  - Smallpox

Single Strand RNA Virus

- + strand
  - Genome used directly as mRNA can be translated immediately
  - Polio
  - Rhinoviruses
- - strand
  - mRNA must be transcribed from genome template
  - Must carry RNA dependent RNA polymerase enzyme
    - RdRp
  - Measles



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Single Strand RNA Viruses

- Nonenveloped
- Picornaviridae
  - Rhinovirus
  - Common cold
  - Poilovirus
- Calciciviridae
  - Norovirus
  - Stomach Flu

- Enveloped + strand
- Togaviridae
  - Rubivirus – rubella
- Flavivirus
  - Yellow fever

- Enveloped - strand
- Rhabdoviridae
  - Rabies
- Filoviridae
  - Ebola
- Orthomyxoviridae
  - Influenza
  - Multiple segments of single stranded RNA

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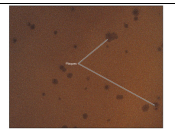
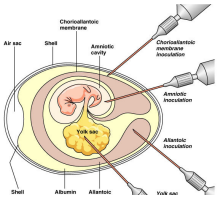
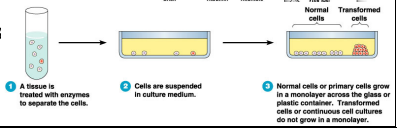
Culturing Viruses



- Viruses must be grown in living cells.
- Bacteria
  - Phages
- Live animals
- Embryonated eggs
  - Vaccine development
- Animal cell cultures





1 A tissue is treated with enzymes to separate the cells.

2 Cells are suspended in culture medium.

3 Normal cells or primary cells grow in a monolayer across the glass or plastic container. Transformed cells or continuous cell cultures do not grow in a monolayer.

Virus Identification

- Cytopathic effects
- Serological tests
  - Detect antibodies against viruses in a patient
  - Use antibodies to identify viruses in neutralization tests,
  - viral hemagglutination
  - Western blot
- Nucleic acids
  - PCR
  - RFLPs

Bacteriophages (Lytic Cycle)

• Attachment	Phage attaches by tail fibers to host cell
• Penetration	Phage lysozyme opens cell wall, tail sheath contracts to force tail core and DNA into cell
• Biosynthesis	Production of phage DNA and proteins
• Maturation	Assembly of phage particles
• Release	Phage lysozyme breaks cell wall

The Lysogenic Cycle

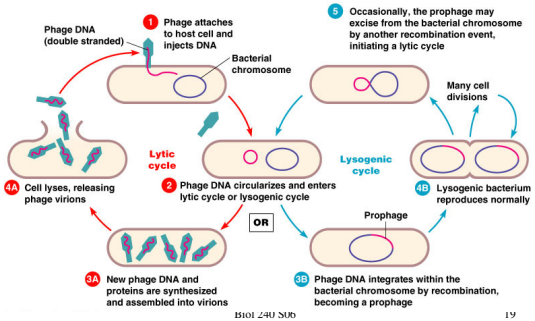
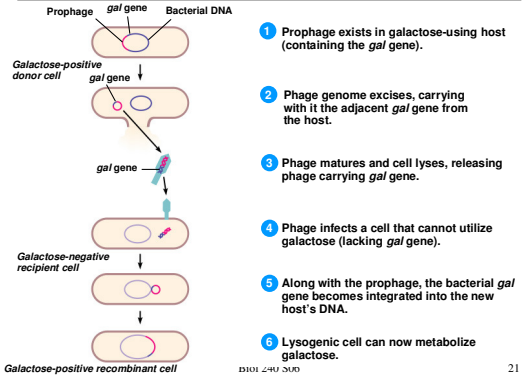


Figure 13.12

Bacteriophage Therapy?

- Literally "Bacteria eaters" or 'phages'
- Specific to particular serotypes of bacteria
- Cannot infect humans
- Most abundant 'organisms' on earth
- Role in combating drug-resistant bacteria?

Specialized Transduction



1. Prophage exists in galactose-using host (containing the *gal* gene).
2. Phage genome excises, carrying with it the adjacent *gal* gene from the host.
3. Phage matures and cell lyses, releasing phage carrying *gal* gene.
4. Phage infects a cell that cannot utilize galactose (lacking *gal* gene).
5. Along with the prophage, the bacterial *gal* gene becomes integrated into the new host's DNA.
6. Lysogenic cell can now metabolize galactose.

Figure 13.13

Animal viruses

- Attachment Viruses attaches to cell membrane receptor
- Penetration By endocytosis or fusion
- Uncoating By viral or host enzymes
- Biosynthesis Production of nucleic acid and proteins
- Maturation Nucleic acid and capsid proteins assemble
- Release By budding (enveloped viruses) or rupture

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Attachment, Penetration, and Uncoating

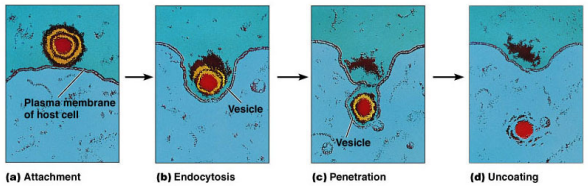

Figure 13.14

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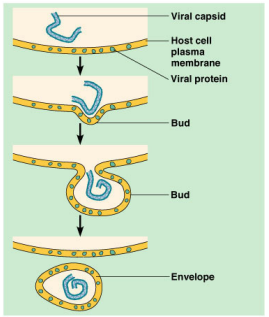
Release of an enveloped virus by budding



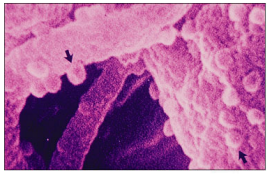
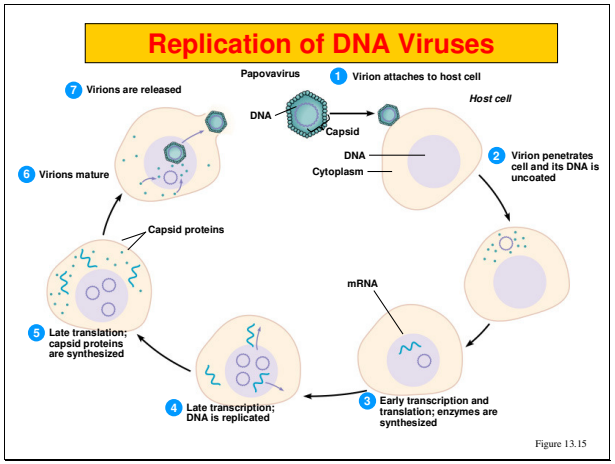
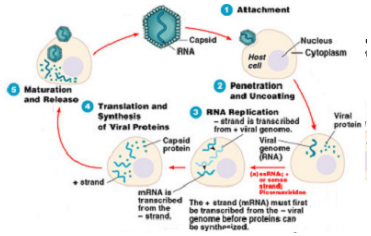


Figure 13.20



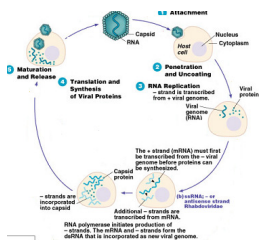
- Viral genome transcribed
- "early proteins"
  - Enzymes for viral replication
- RdRp
  - Synthesizes – stand
  - template for making new + strands
- "late proteins"
  - capsid proteins

+ RNA or Sense Strand = mRNA



- Strand RNA Viruses

- RNA dependent RNA Polymerase
- Uses – strand to make + strand
- + strand (mRNA) transcribed into viral proteins



Retrovirus Replication

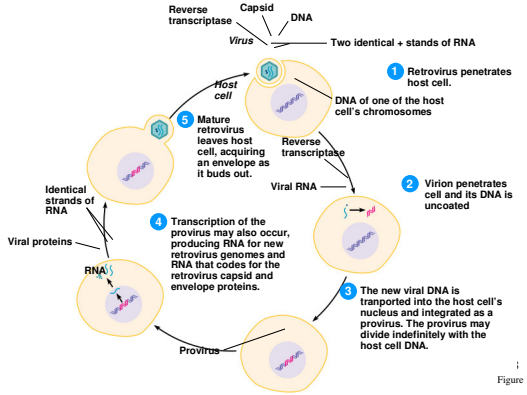


Figure 13.19

Oncogenes and Cancer

- Activated oncogenes transform normal cells into cancerous cells.
- Transformed cells
  - increased growth
  - loss of contact inhibition
  - tumor specific transplant antigens
  - T antigens.
- The genetic material of oncogenic viruses becomes integrated into the host cell's DNA.

Oncogenic Viruses

- Oncogenic DNA Viruses
  - Herpesviridae
    - HHV-4, Burkitt's Lymphoma
    - HHV -8 Kaposi's sarcoma
  - Papilliomaviridae
    - HPV 16 HPV 18
    - Cervical cancer
  - Hepadnaviridae
  - Hepatitis B- Liver cancer
- Oncogenic RNA viruses
  - Flaviviridae
    - Hepatitis C – Liver cancer
  - Retroviridae
    - HTLV 1
    - Human T-Lymphotrophic Virus
    - Leukemia

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Latent v Persistent Infections

- Latent Viral Infections
  - Virus remains in asymptomatic host cell for long periods
    - Cold sores, shingles
- Persistent Viral Infections
  - Disease processes occurs over a long period, generally fatal
    - Subacute sclerosing panencephalitis (measles virus)

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Common Cold

- + Single Strand RNA
- Binds to receptor on mucous membrane of nose
  - Lower temperatures 91°F
- Acute Infection
- High virulence 1 virus particle sufficient to cause infection
- Replication within 8 hours producing thousands of infectious particles
- Infection over before immune system able to produce antibodies
- Susceptible to re-infection

Cytopathic Effects

- Rhinovirus RNA possesses initiation sequence Rhinovirus protein disrupts normal cap-dependent initiation shutting down protein synthesis of cellular (capped) mRNA
- Ribosomes only synthesize viral proteins
- Cells die

Prions

- Infectious proteins
  - Inherited and transmissible by ingestion, transplant, & surgical instruments
- All are fatal
- Kuru
- Sheep scrapie,
- Creutzfeldt-Jakob disease
- Mad cow disease
  - Bovine Spongiform Encephalopathy
- Fatal familial insomnia

Prions

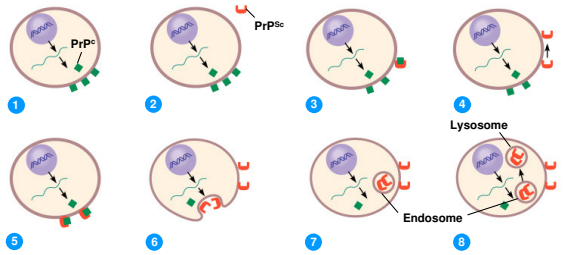
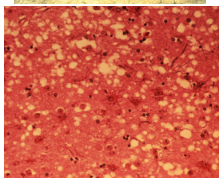


Figure 13.21

The UK BSE Outbreak

- Bovine Spongiform Encephalopathy
  - 179,000 cases 1985-89
  - 4.4 million cattle culled
- Cows fed protein supplement containing Sheep spines infected with Scrapie prion
- New variant CJD
- Creutzfeldt-Jakob disease.
  - 165 cases in UK
  - Still no evidence for link



Vaccines

- Introduce viral antigen (or bacterial, or toxin) into body
- Muscular
- Oral
- Nasal
- Stimulate formation of antibodies
- Cell mediated immunity

Vaccine History

- Variolation: Inoculation of smallpox into skin (18th century)
- Vaccination: Inoculation of cowpox (Vaccina) into skin
  - Edward Jenner

Vaccination

- Prevention better (and cheaper)than cure
- Herd Immunity
- Epidemics
- Eradication
  - Small pox
  - Polio?
  - Measles ?

Attenuated Whole-Antigen Vaccines

- Living, but weakened virus
  - Vaccines require refrigeration
- Lifelong immunity
- 95% effective
- Living virus replicates in body
- Polio - Sabin

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Inactivated Whole-Agent Vaccines

- Microbes killed
- Protein structure not altered
- Polio - Salk
- Rabies
- Hepatitis A
- Flu
- Cholera
- Does NOT provide as long lived immunity

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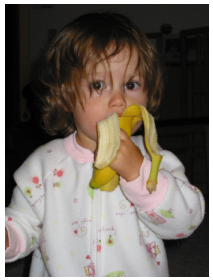
Toxoids

- Toxoids
- Inactivated toxins
- Vaccines → Antibodies to toxin
- Dtap
- Diphtheria
- Tetanus
- Acellular Pertussis

Subunit and Conjugate Vaccines

- Subunit Vaccines
  - Only use antigenic fragments – proteins
  - Recombinant bacteria produce antigens of pathogen
- Hepatitis B
  - Yeast synthesizes viral protein
- Conjugate vaccines
- Improves immune response to a poorly antigenic substance
  - Capsule fragment + protein
  - Pneumococcal Conjugate Vaccine
  - Hib vaccine

Development of New Vaccines

- Fear of Litigation
- Allergic reaction
  - Flu vaccines and eggs
- High cost but low Profit
- Culturing Live Viruses
- Recombinant Vaccines
- Edible Vaccines…?