Viruses, viroid & prions
General Characteristics

- Obligatory intracellular parasites - do not possess mechanisms to replicate outside of a host cell
- Contain RNA or DNA (not both)
- Protein coat - sometimes an envelope
- Cause synthesis of specialized structures that can transfer viral nucleic acid to other cells
Host Range

- All living organisms can be infected by specific viruses
- Most viruses can infect only specific cells determined by:
  - requirements for attachment to host cell (receptor sites)
  - and metabolic needs w/in cell in order to multiply
Viral Size

- Length 20 - 14,000 nm
- Much smaller than bacteria - therefore filterable (see intro for discovery of infectious agent that could pass through porcelain filter; also see that many originated in animals
Enveloped virus

- Envelope - lipid, protein, carbohydrate, may have attachment spikes; also nonenveloped viruses

- Virus surface proteins interact with host antibodies; but they may mutate! Escape detection by antibody
Biosynthesis of DNA viruses

- Viral enzymes used to replicate DNA inside eukaryotic cell’s nucleus
- Host enzymes synthesize viral protein - enter nucleus where virions are assembled
- Adeno-, papo-, herpes, hepadna viruses
Biosynthesis of RNA viruses

- Attachment, penetration and uncoating
- RNA “sense” strand forms complementary “antisense” strand
Multiplication of Retrovirus

- Attachment, penetration and uncoating
- Reverse transcriptase forms DNA from RNA; provirus incorporates in host chromosome
- May be latent or produce new viruses
Prions

- Proteinaceous infectious particle
- 9 neurological diseases- spongiform encephalopathies
- PrP\textsuperscript{C} in normal DNA
- PrP\textsuperscript{Sc} (abnormal) can change PrP\textsuperscript{C} to PrP\textsuperscript{Sc} on contact >> plaques
RNA VIRUSES
REOVIRIDAE

- REO = Respiratory Enteric Orphan Virus
- Non-enveloped
- Icosahedral
- RNA ds
- Human Diseases
  - Rotavirus
  - Colorado Tick Fever
    - Acute febrile illness
    - Tick vector
Rotavirus

- World wide infection
- Fecal-oral spread
- Incubation: 1-3 days
- Diarrhea
- Diagnosis
  - ELISA
  - Latex Agglutination
- Prevention
  - Hygiene
  - Water sanitation
CALICIVIRIDAE

- Calicus = Cup shaped
- Non-enveloped
- Icosahedral
- Linear ss + RNA
- Human Diseases
  - Norwalk Virus
  - Hepatitis E
Calicivirus

- Norwalk Virus
  - Summer diarrhea
  - Epidemic
  - Gastroenteritis
  - V/D
  - Institutions
  - ID virus in stool

- Hepatitis E
  - NonA-NonB
  - Endemic
  - Hepatitis
  - Acute, self limiting
  - Fecal-oral
  - IgM or ID virus in stool
PICORNAVIRIDAE

- Pico = small
- Nonenveloped
- Icosahedral
- RNA + ss
- Human Diseases
  - Polio
  - Coxsackie A, B
  - ECHO
    - Rhinovirus
    - Hepatitis A
Hepatitis A

- Infectious Hepatitis
- Milder disease than Hepatitis B
- No chronic form
- Incubation: 2-5 weeks
- Virus excreted in stool, so fecal-oral transmission
- Dx: IgM
Poliomyelitis

- Transmission: fecal-oral
- Throat -> LN -> Ileum -> Blood -> CNS
- Phases
  - Asymptomatic: 90%
  - Non-paralytic
  - Paralytic: 2-3%, causes 75% of paralysis
- Dx: virus in feces, secretions
- Prevention: Vaccine
  - Salk (IPV, killed)
  - Sabin (OPV, modified live)
Rhinovirus

- Common cold virus: 50%
- Transmission: inhalation
- Incubation: 1-3 days
- Symptoms
  - Sore throat
  - Mucopurulent nasal discharge
- Complications: predispose to secondary bacterial infections
TOGAVIRIDAE

- Toga = coat
- Spiked envelope
- Icosahedral
- Linear ss+RNA
- Human diseases
  - Encephalitis
    - (VEE, WEE, EEE)
  - Rubella
Togavirus

- **Rubella**
  - German Measles
  - Droplet
  - 2-3 week incubation
  - Rash
    - Facial
    - Spreads to body
    - Changes hourly
- **Complications**
  - Congenital defects
    - Nervous
    - Heart
- **Prevention:** MMR
CORONAVIRIDAE

- Corona = crown
- Enveloped
- Helical
- Linear RNA + ss
- Human Diseases
  - Common cold (20%)
  - SARS
Severe Acute Respiratory Syndrome (SARS)

- Respiratory Droplet
  - Direct
  - Indirect
- 2-10 day incubation
- Cough -> Pneumonia
- Stable in environment for days
- Dx: PCR
- Tx: supportive
- Prevention: avoid contact, disinfect
FLAVIVIRIDAE

- Flavus = yellow
- Enveloped
- Helical
- Linear RNA ss +
- Human Diseases
  - Hepatitis
  - Encephalitis
  - Hemorrhagic Fever
Flavivirus

- Hepatitis C
  - Endemic
  - Parental: blood
  - 6-8 week incubation
  - Mild form
  - Chronic -> cancer
  - Dx: IgG, PCR
  - Tx: Interferon
Flaviviridae

- Hepatitis
  - Yellow Fever
  - Hepatitis G
    - Acute
    - Persistent
  - Co-infection with Hepatitis C
  - Parental: blood

- Encephalitis
  - Japanese Complex
  - St. Louis
    - Acute
    - Inflammatory
    - Vector: mosquito
    - 4-21 days incubation
Flavivirus

- West Nile Virus
  - Acute
  - Febrile
  - Hemorrhagic
  - Vector: mosquito
  - 3-14 days incubation
  - Dx: IgM, ELISA
  - Tx: Supportive
ASTROVIRIDAE

- Astro = Star
- Nonenveloped
- RNA ss+
- 7 Human Serotypes
- Diarrhea
BUNYAVIRIDAE

- Named after location of first viral isolation
- Spiked, enveloped
- Helical
- Circular ss-RNA
- Human Disease
  - Encephalitis
  - Respiratory
  - Hemorrhagic Fever
Bunyavirus

- Hanta virus
  - Adult Respiratory Disease
  - 1-3 weeks incubation
  - Transmission: deer mice
  - Symptoms
    - SOB
    - N/V
    - pain
  - Tx: supportive
  - Prevention: rodent control, disinfect
ORTHOMYXOVIRIDAE

- Myxo = mucus
- Spiked envelope (HA,N)
- Helical capsid
- Segmented linear ss-RNA
- Human Diseases
  - Influenza A
  - Influenza B
  - Influenza C
Orthomyxovirus

- **Influenza**
  - Range of symptoms from mild to severe
  - Droplet
    - Direct
    - Indirect
  - 1-3 days incubation
  - Reservoir: Humans
  - Treatments
    - Vaccination
    - Drugs
  - Complications
    - Recombinant due to segmented RNA
    - Secondary bacterial infections
    - Viral Superinfection with Adenovirus

Influenza Treatments
Inhibit Neuraminidase
- Relenza (IN)
- Tamiflu (PO)
PARAMYXOVIRIDAE

- Similar to Orthomyxoviruses
- Spiked Envelope
  - HA
  - N
  - Fusion
- Helical
- Segmented linear ss – RNA
- Human Diseases
  - Respiratory
  - Epithelial
Paramyxovirus: Respiratory

- Parainfluenza
  - 4 types
  - Pediatric infection
  - Symptoms
    - Fever
    - Coryza
    - Barking cough
    - Airway obstruction
  - Droplet
- Tx: supportive

- Respiratory Syncytial Virus (RSV)
  - Infants
  - Pneumonia
  - Symptoms
    - Cold like
    - Fever
    - Coryza
    - Cough
    - Wheeze
  - Droplet
  - Tx: supportive
Paramyxovirus: Epithelial

- **Mumps**
  - Glandular
  - Droplet transmission
  - 21 day incubation
  - Inflammation
  - Complications
    - Meningitis
    - Orchitis
  - IgM
  - Tx: symptomatic
  - Prevention: MMR

- **Measles**
  - Epithelial mucosal linings
    - Skin -> rash
    - Respiratory
    - GI
  - Droplet transmission
  - 10-12 days incubation
  - Desquamation
  - Highly infectious
  - Tx: symptomatic
  - Prevention: MMR
RHABDOVIRIDAE

- Rhabdo = rod like
- Spiked, enveloped
  - Hemagglutinin
- Helical
- RNA ss-
- Human Disease
  - Vesicular Stomatitis
  - Rabies
Rhabdovirus

- Lyssa virus
  - Rabies
    - Encephalitis
    - Direct
    - 3-8 weeks incubation
    - Replication
      - Local
      - CNS
      - Salivary
    - Reservoir
      - Bats
      - Foxes
      - Skunks
    - Clinical
      - Furious
      - Dumb

Electron micrograph of rabies virus in brain cells at 64,000x magnification. The bullet-shaped particles surrounding the smooth gray circle are rabies. The circle itself is the Negri body, which can be seen with a light microscope. Courtesy of Dr. F.A. Murphy, UC Davis.
FILOVIRIDAE

- Filo = filamentous
- Spiked, enveloped
- Helical
- Linear ss – RNA
- Pleomorphic shape
  - Filament, branched, U-shape, Circular
- Human Disease
  - Acute Hemorrhagic fever
    - Marburg Virus
    - Ebola Virus
Ebola virus

- Acute hemorrhagic fever
- 4-16 day incubation
- Symptoms
  - Fever
  - V/D
  - Rash
  - Hemorrhage from all open body cavities
  - Death due to shock from fluid and blood loss
ARENADVIRIDAE

- Arenosus = sand
- Enveloped
- Helical
- Segmented linear ss-RNA

Human Disease
- Hemorrhagic fever
  - Lassa (Old world)
- Lymphocytic choriomeningitis
  - New world arenavirus
RETROVIRIDAE

- Retro = reverse
- RNA dependent DNA polymerase (RT)
- Spiked envelope
- Icosahedral
- 2 linear ss + RNA (diploid virus)

Human Diseases
- HTLV: leukemia
- HIV: AIDS
Retroviridae

- Human T-Lymphocytic Virus (HTLV-1)
  - Adult Leukemia
  - Aggressive Tumor
  - Latent
  - Infiltrates
    - Skin
    - brain
  - Transmission
    - Horizontal
      - Blood
      - Sexual Intercourse
    - Vertical
      - Breast milk
Human Immunodeficiency Virus
Unclassified Viruses

- Hepatitis D
  - Defective
  - Incomplete ss RNA
  - Enveloped
  - Really a viroid
  - Requires coinfection with Hepatitis B
Zoonoses

- Disease that humans can acquire from animals
- Viral examples
  - Marburg (monkeys)
  - Pox (cow pox, pseudocowpox, monkeypox)
  - Rabies (warm blooded mammals)
  - Influenza A
  - Lassa (rodents, bats)
  - Hanta virus: pulmonary (rodents)
Viral Vaccines

- Live / Attenuated
  - Measles
  - Mumps
  - Rubella
  - Polio (oral)
  - Yellow Fever
  - VZV

- Killed / Viral Protein
  - Hepatitis A
  - Hepatitis B
  - Rabies
  - Polio (Salk)
Antiviral Chemotherapy

- Inhibits Viral DNA-dependent DNA polymerase
  - Herpes
- Inhibits DNA replication and transcription
  - Herpes
- Interferes with penetration or viral uncoating
  - Influenza A
- Inhibits translation of late mRNA
  - Smallpox
- Inhibits reverse transcriptase
  - Aids
- Inhibits Protein synthesis
  - Genital Warts
Viruses in Human Infections and Diseases

DNA or RNA molecules are surrounded by capsid; obligate parasites that enter a cell, instruct its genetic and molecular machinery to produce and release new viruses.

All DNA viruses are double-stranded except for parvoviruses, which have ssDNA.

All RNA viruses are single-stranded except for dsRNA reoviruses.
Medical Considerations in Viral Diseases

Viruses are limited to a particular host or cell type.
Most DNA viruses are budded off the nucleus.
Most RNA viruses multiply in and are released from the cytoplasm.
Viral infections range from asymptomatic to mild to life-threatening.
Many viruses are strictly human in origin, others are zoonoses transmitted by vectors.
Course of viral disease: invasion at portal of entry and primary infection; some viruses replicate locally, others enter the circulation and infect other tissues.

Common manifestations: rashes, fever, muscle aches, respiratory involvement, swollen lymph nodes.

Body defenses: combined action of interferon, antibodies and cytotoxic T cells; frequently results in lifelong immunity.
Many viral infections have rapid course; lytic cycle •
Some viruses establish long-term **persistent** •
infections that last many years or a lifetime.
2 types of persistent infections: •
**chronic infections** – virus is detectable in tissue –
samples, multiplying at a slow rate; symptoms mild or absent
**latent infections** – after a lytic cycle, virus enters a –
dormant phase; generally not detectable, no symptoms; can reactivate and result in recurrent infections
Some persistent viruses are **oncogenic**. • Several viruses can cross the placenta • causing developmental disturbances and permanent defects – **teratogenic**.

Diagnosis of viral diseases – symptoms, • isolation in cell or animal culture, serological tests for antibodies; some tests for antigens
Survey of DNA Viruses

Animal viruses are categorized according to • nucleic acid, capsid, and presence or absence of envelope.

7 DNA families, 15 RNA families •

DNA viruses causing human disease: •
enveloped DNA viruses —
nonenveloped DNA viruses —
nonenveloped ssDNA viruses —
TABLE 24.1

DNA Virus Groups That Infect Humans

DNA Viruses

- Enveloped
  - Double-stranded genome
    - Poxviruses
      - Herpesviruses
    - Herpesviruses
- Nonenveloped
  - Double-stranded genome
    - Adenoviruses
      - Polyomaviruses
        - Papillomaviruses
    - Polyomaviruses
      - Parvoviruses
Poxviruses: Classification and Structure

- Produce eruptive skin pustules called pocks or pox, that leave scars
- Largest and most complex animal viruses
- Have the largest genome of all viruses
- dsDNA
- Multiply in cytoplasm in factory areas
  - variola – cause of smallpox
  - vaccinia – closely related virus used in vaccines
  - monkeypox
  - cowpox
Smallpox

First disease to be eliminated by vaccination
Exposure through inhalation or skin contact
Infection associated with fever, malaise, prostration, and a rash
variola major – highly virulent, caused toxemia, shock, and intravascular coagulation
variola minor – less virulent
Routine vaccination ended in U.S. in 1972.
Vaccine reintroduced in 2002 for military and medical personnel
Molluscum Contagiosum

In endemic areas, it is primarily an infection of children.

Transmitted by direct contact and fomites

In US, most commonly an STD

Lesions are small, smooth macules in genital area and thighs.

AIDS patients suffer an atypical form which attacks the skin of the face and forms tumorlike growths.

Treatment: freezing, electric cautery, chemical agents
Other Poxviruses

Many mammalian groups host some poxvirus –
• cowpox, rabbitpox, mousepox, elephantpox.
Humans are susceptible to monkeypox and
• cowpox.
Monkeypox in humans – skin pocks, fever, swollen
• lymph nodes
Cowpox in humans – rare, usually confined to
• hands; other cutaneous sites can be involved
The Herpesviruses: Common, Persistent Human Viruses

All members show latency and cause recurrent infection; viral DNA forms episome.

Clinical complications of latency and recurrent infections become more severe with advancing age, cancer chemotherapy, or other conditions that compromise the immune defenses.

Common and serious opportunists among AIDS patients

Large enveloped icosahedral dsDNA

Replicates within nucleus
Glycoprotein spikes  Envelope  DNA core

(a)

(b)

© Kathy Park Talaro
Herpesviruses

Large family; 8 infect humans •
HSV-1 – herpes simplex 1
HSV-2 - herpes simplex 2
VZV – varicella zoster virus
CMV - cytomegalovirus
EBV – Epstein-Barr virus
HHV-6 – herpevirus 6 - roseola
HHV-7 - herpevirus 7
HHV-8 - herpevirus 8
Herpes Simplex Viruses

Humans susceptible to 2 varieties • HSV-1 - usually lesions on the oropharynx, • cold sores, fever blisters occurs in early childhood – HSV-2 - lesions on the genitalia, possibly • oral occurs in ages 14-29 – can be spread without visible lesions –
Epidemiology

Transmission by direct exposure to secretions containing the virus; active lesions most significant source; genital herpes can be transmitted in the absence of lesions

HSV multiplies in sensory neurons, moves to ganglia

- HSV-1 enters 5th cranial nerve
- HSV-2 enters lumbosacral spinal nerve trunk ganglia

Recurrent infection is triggered by various stimuli — fever, UV radiation, stress, mechanical injury.

Newly formed viruses migrate to body surface, producing a local skin or membrane lesion.
Latency and routes of recurrence
Type 1 Herpes Simplex in Children and Adults

Herpes labialis – fever blisters, cold sores; most common recurrent HSV-1 infection; vesicles occur on mucocutaneous junction of lips or adjacent skin; itching and tingling prior to vesicle formation; lesion crusts over in 2-3 days and heals

Herpetic gingivostomatitis – infection of oropharynx in young children; fever, sore throat, swollen lymph nodes

Herpetic keratitis – ocular herpes – inflammation of eye; gritty feeling in the eye, conjunctivitis, sharp pain, and sensitivity to light
Type 2 Herpes Infections

Genital herpes – herpes genitalia – starts with • malaise, anorexia, fever, and bilateral swelling and tenderness in the groin; clusters of sensitive vesicles on the genitalia, perineum, and buttocks; urethritis, painful urination, cervicitis, itching; vesicles ulcerate

Recurrent bouts usually less severe, triggered by • menstruation, stress, and concurrent bacterial infection
Herpes of the Newborn

HSV-1 and HSV-2 •
Potentially fatal in the neonate and fetus •
Infant contaminated by mother before or during birth; hand transmission by mother to infant
Infection of mouth, skin, eyes, CNS •
Preventative screening of pregnant women; delivery by C-section if outbreak at the time of birth
Miscellaneous Herpes Infections

Herpetic whitlow - HSV-1 or HSV-2 can penetrate a break in the skin and cause a localized infection; usually on one finger; extremely painful and itchy

HSV-1 encephalitis – rare complication but most common sporadic form of viral encephalitis in the U.S.

Those with underlying immunodeficiency are prone to severe, disseminated herpes.
Diagnosis, Treatment, and Control of Herpes Simplex

Vesicles and exudate are typical diagnostic symptoms, scrapings from base of lesions showing giant cells, culture and specific tests for diagnosing severe or disseminated HSV; direct fluorescent antibody tests

Treatment: acyclovir, famciclovir, valacyclovir; topical medications
Varicella-Zoster Virus (VZV)

Causes chickenpox and shingles •
Humans only natural host •
Transmitted by respiratory droplets and contact •
Primary infection – chickenpox – characteristic vesicles •
Virus enters neurons and remains latent •
Later, reactivation of the virus results in shingles with •
vesicles localized to distinctive areas, dermatomes.
More common in older patients •
Treatment: treat symptoms in uncomplicated • infections; acyclovir, famciclovir, interferon for systemic disease
Live attenuated vaccine for chickenpox and shingles •
Herpes zoster virus is activated in ganglion by stress.
Viruses migrate down sensory nerve to skin.

Spinal cord