RNA Viruses

Assigned to one of 12 families based on envelope, capsid, and structure of RNA genome

Orthomyxoviruses

- Enveloped, segmented ssRNA
- 2 types of envelope glycoprotein spikes
  - Hemagglutinin (HA) – binds to host cells
  - Neuraminidase (NA) – hydrolyzes mucus & assists viral budding & release
- Genome constantly changes
  - Antigenic drift – minor change caused by mutations
  - Antigenic shift - major alteration occurring when segments recombine

I have a little bird
Her name is Enza
I opened the window
And in flew Enza

Nursery Rhyme, 1918

Influenza type A

- Acute, highly contagious respiratory illness
- Seasonal, pandemics
- Among top 10 causes of death in US
- Respiratory transmission
- Binds to ciliated cells of respiratory mucosa
- Causes rapid shedding of cells, stripping the respiratory epithelium, severe inflammation
- Fever, headache, myalgia, pharyngeal pain, shortness of breath, coughing
- Treatment: amantadine, rimantadine, zanamivir & oseltamivir (Tamiflu)
- Annual trivalent vaccine
Bunyaviruses

- Transmitted zoonotically; cause periodic epidemics; extremely dangerous; biosafety level 4 viruses
- Often transmitted by insects and ticks
- American bunyavirus is a hantavirus, Sin Nombre - emerging disease; high fever, lung edema, and pulmonary failure; 33% mortality rate
- Carried by deer and harvest mice; transmitted via airborne dried animal waste

Paramyxoviruses

- Enveloped ssRNA
  - Paramyxovirus (parainfluenza, mumps virus)
  - Morbillivirus (measles virus)
  - Pneumovirus (respiratory syncytia virus)
- Respiratory transmission
- Envelope has H, N & F spikes
- Virus causes infected cells to fuse with neighboring cells - syncytium or multinucleate giant cells form

Parainfluenza

- As widespread as influenza but more benign
- Respiratory transmission
- Seen mostly in children
- Presents as minor cold, bronchitis, bronchopneumonia, croup
- No specific treatment available

Mumps

- Epidemic parotitis
- Self-limited, associated with painful swelling of parotid salivary glands
- Humans are the only reservoir
- 40% of infections are subclinical
- 300 cases in US/year
- Incubation 2-3 weeks; fever, muscle pain & malaise, classic swelling of both cheeks
- In 20-30% of infected males, epididymis & testes become infected; sterilization is rare
- Live attenuated vaccine MMR

Measles

- Caused by Morbillivirus
- Also known as red measles & rubeola
- Very contagious
- Transmitted by respiratory aerosols
- Humans are the only reservoir
- Fewer than 100 cases/yr in US
- Virus invades respiratory tract
- Sore throat, dry cough, headache, conjunctivitis, lymphadenitis, fever, oral lesions
- Rash
**Measles & Complications**

- Most serious complication is subacute sclerosing panencephalitis (SSPE), a progressive neurological degeneration of the cerebral cortex, white matter & brain stem
- 1 case in a million infections
- Involves a defective virus spreading through the brain by cell fusion & destroying cells
- Leads to coma & death in months or years
- Attenuated viral vaccine MMR

**Respiratory Syncitial Virus**

- Also called Pneumovirus
- Infects upper respiratory tract & produces giant multinucleate cells
- Most prevalent cause of respiratory infection in children 6 months or younger; those most susceptible to serious disease
- Epithelia of nose & eye are portals of entry
- Replicates in nasopharynx
- Rhinitis, wheezing, otitis, croup, bronchiolitis, pneumonia
- Treatment: Synagis, a monoclonal antibody that blocks attachment, ribavirin

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**Rabies**

- Rhabdovirus family
- Genus Lyssavirus
- Bullet-shaped virions
- Enveloped
- Slow, progressive zoonotic disease
- Virus enters through bite, grows at trauma site for a week, enters nerve endings & advances toward the ganglia, spinal cord & brain

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**Coronavirus**

- Relatively large RNA viruses with distictively spadce spikes on their envelopes
- Common in domesticated animals
- 3 types of human coronaviruses have been characterized
  - HCV causes a cold
  - an enteric virus
  - Severe Acute Respiratory Syndrome (SARS)
  - airborne transmission
  - 10% of cases fatal
Severe Acute Respiratory Syndrome-Associated Coronavirus (SARS)

- Newly emerging disease – 2002
- Transmitted through droplet or direct contact
- Fever, body aches, and malaise
- May or may not experience respiratory symptoms with breathing problems; severe cases can result in respiratory distress and death
- Diagnosis relies on exclusion of other likely agents
- Treatment is supportive

Rubella

- Caused by Rubivirus, a Togavirus
- ssRNA with a loose envelope
- German measles
- Transmitted through contact with respiratory secretions

Rubella

- Postnatal rubella – malaise, fever, sore throat, lymphadenopathy, rash, generally mild
- Congenital rubella – infection during 1st trimester most likely to induce miscarriage or multiple defects such as cardiac abnormalities, ocular lesions, deafness, mental & physical retardation
- Attenuated viral vaccine MMR

Hepatitis C Virus (HCV)

- Flavivirus
- Acquired through blood contact – blood transfusions, needle sharing by drug abusers
- Infections with varying characteristics – 75-85% will remain infected indefinitely; possible to have severe symptoms without permanent liver damage; more common to have chronic liver disease, without overt symptoms
- Cancer may also result from chronic HCV infection
- Treatment with interferon and ribavirin to lessen liver damage; no cure
- No vaccine

Arboviruses

- Viruses that spread by arthropod vectors – mosquitoes, ticks, flies, & gnats
- 400 viruses
- Togaviruses, flaviviruses, some bunyaviruses & reoviruses
- Most illnesses caused by these viruses are mild fevers, some cause severe encephalitis
- Dengue fever, western & eastern equine encephalitis, yellow fever
Retroviruses

- Enveloped, ssRNA viruses
- Encode reverse transcriptase enzyme which makes a DNA copy of their RNA genome
- Human Immunodeficiency Virus (HIV) the cause of Acquired Immunodeficiency Syndrome (AIDS)
- HIV-1 & HIV-2
- T-cell lymphotropic viruses I & II - leukemia

AIDS

- First emerged in early 1980s
- HIV-1 & HIV-2 are not closely related
- HIV-1 may have originated from a chimpanzee virus
- 1983 first documented case of AIDS
- HIV is found in blood, semen, & vaginal secretions
- HIV is transmitted by sex, sharing needles, and mother to child
- HIV does not survive long outside of the body unless it is sheltered

HIV

- Attacks the T helper cells & macrophages
- In 2006, the number of infected individuals worldwide was estimated to be 45 million with ~1 million in the U.S.
- First signs of AIDS are opportunistic infections such as *Pneumocystis carinii* pneumonia (PCP) and cancers such as Kaposi sarcoma

Risk categories

- Homosexual or bisexual males -- 45%
- Intravenous drug users -- 30%
- Heterosexual partners of HIV carriers -- 11%
- Blood transfusions & blood products -- since testing, no longer a serious risk
- Inapparent or unknown risk -- 9% - (due to denial, death, unavailability)
- Congenital or neonatal -- can be reduced with antiviral drugs
- Medical & dental personnel -- 1/500 by accidental needle-stick
Non-enveloped ssRNA Viruses

- Picornaviruses
  - Enterovirus – poliovirus, HAV
  - Rhinovirus - rhinovirus
- Calciviruses
  - Norwalk agent (Norovirus) – common cause of viral gastroenteritis (cruise ships)

Poliovirus

- Resistant to acid, bile, & detergents
- Can survive stomach acids
- Virus is ingested
- Grows in oropharynx & intestine
- Most infections are mild
- If viremia persists, virus spreads to spinal cord & brain
- Invasion of motor neurons causes flaccid paralysis
- Decades later post-polio syndrome (PPS)

Polio

- Inactivated polio vaccine (IPV) Salk vaccine – released 1955
- Oral polio vaccine (OPV) Sabin vaccine, attenuated virus
- Both are trivalent
- WHO goal of eradicating polio by 2005 not achieved

Hepatitis A Virus

- Causes short-term hepatitis
- Fecal-oral transmission
- Most infections subclinical or vague, flu-like symptoms occur, jaundice is seldom present
- Inactivated viral vaccine
- Attenuated viral vaccine
- Pooled immune serum globulin

Human Rhinovirus

- 110 serotypes
- Causes the common cold
- Sensitive to acidic environments
- Optimum temperature is 33°C

Calciviruses

- Norwalk agent best known; believed to cause 1/3 of all viral gastroenteritis cases
- Transmitted by fecal-oral route
- Infection in all ages at any time of year
- Acute onset, nausea, vomiting, cramps, diarrhea, chills
- Rapid and complete recovery, but virus may be shed for ~10 days!
Pathogenesis of HIV

- HIV enters through mucous membrane or skin and travels to dendritic phagocytes beneath the epithelium, multiplies and is shed
- Virus is taken up and amplified by macrophages in the skin, lymph organs, bone marrow, and blood
- HIV attaches to CD4 and coreceptor; HIV fuses with cell membrane
- Reverse transcriptase makes a DNA copy of RNA
- Viral DNA is integrated into host chromosome (provirus)
- Can produce a lytic infection or remain latent

Progression of HIV disease

- Initial infection – mononucleosis-like symptoms that soon disappear
- Asymptomatic phase 2-15 years (avg. 10)
- Antibodies are detectable 8-16 weeks after infection
- HIV destroys the immune system
- When CD4 T cell levels fall below 200/µL symptoms appear including fever, swollen lymph nodes, diarrhea, weight loss, neurological symptoms, opportunistic infections & cancers

HIV

- Treatments
  - Inhibit viral enzymes: reverse transcriptase, protease, integrase
  - Inhibit fusion
  - Inhibit viral translation
- No effective vaccine, yet
- Prevention
  - Monogamous sexual relationships
  - Condoms
  - Universal precautions
Reoviruses

- Non-enveloped, segmented dsRNA viruses
- Inner & outer capsid
- Rotavirus - causes 50% of cases of diarrhea & death of over 600,000 children
  - usually mild in US
  - two effective oral vaccines currently available
- Reovirus - not a significant human pathogen