

## Viruses

### General Characteristics

- Require LIVING cells for growth and replication
- Have either DNA or RNA
- Multiply by separate synthesis of nucleic acid and protein, combine to form virus particles
- Size varies from 10 nm-300 nm

### What are Viruses Made of?

#### Basic Components:

- Nucleic acid: infectious genetic material
- Protein coat: protective
- Surface Antigens: protein or carb, highly variable

### Replication - HSV-1

1. Adsorption
2. Penetration and Uncoating
3. Nucleic Acid and protein synthesis
4. Assembly
5. Release - whole cell is destroyed, or release through cell wall

### Replication- West Nile Virus

1. Adsorption
2. Penetration and Uncoating
3. Nucleic acid and protein synthesis
4. Assembly
5. Release

### How to Detect Viral Infections

1. Detect the virus itself
2. Detect the immune response.. Antibodies against the virus

### Viral Diagnosis

- A. Detection in clinical specimens
  1. Visualization by electron microscopy
  2. Cell culture (cytopathic effects, hemagglutination, immunofluorescence)
- B. Detection of patient's immune responses
  1. Antibody detection, presence or absence (ELISA)
    - a. IMMUNITY TEST- if you have made or not antibodies
  2. Rise in antibody titre or high antibody titre
    - a. DIAGNOSTIC TEST - how much antibodies were made

## Respiratory Viruses

- Respiratory disease
- Different families
  1. Influenza viruses
  2. Parainfluenza viruses
  3. Respiratory syncytial viruses
  4. Rhinoviruses
  5. Adenoviruses
  6. Echoviruses, coxsackie viruses, herpes viruses (occasional respiratory tract infection)

### 1. Influenza Viruses

- Influenza virus type A: major epidemics
- Influenza virus type B: milder disease
- Produce haemagglutinin (diagnostic) - can use a hemagglutination
- Frequent recombination
  - = high antigenic variability
  - = pandemics
- Clinical:
  - Fever, variable variable respiratory symptoms
  - Infants and elderly more susceptible
- Diagnosis:
  - Throat washings, nasopharyngeal aspirate inoculated into cell culture
- Serum:
  - Paired sera (acute-almost dead and convalescent stage-getting better)
- Prevention:
  - **Annual vaccination** especially for high risk groups

### What about disease severity?

- Greater disease burden in <25 years than in >65 years
  - Unusual for seasonal flu
- Certain groups have risk of complications
  - Pregnant women, asthma, diabetes, immune suppression, heart disease, kidney disease
  - Same as for flu season

### What does the virus look like?

- Has been termed “swine” flu
- Influenza genome has 8 segments
- 2009 H1N1 segments
  - 3 from classical swine
  - 2 from asian swine
  - 2 from avian
  - 1 from human

## H1N1 2009 Vaccine

- Vaccination is major effort of PHAC to fight pandemic flu
- Canada has a dedicated vaccine manufacturer
- Adjuvanted vs non adjuvanted vaccine
  - Why adjuvant?
    - To reduce the amount of vaccine protein per dose
  - Why new adjuvant?
    - Existing adjuvants have never worked well for flu shots
  - Why controversial?
    - Little data on adjuvant in children, pregnant women
    - New adjuvant had not been used in other vaccines

## 2. Parainfluenza viruses

- **Infants and young children**
- Respiratory infection that could have serious complications
- **Croup** (barking cough, high pitch sound on inhalation)
- Bronchiolitis, bronchopneumonia
- **No vaccine**

## 3. Respiratory Syncytial Virus

- **Major respiratory pathogen for children < 2 years old**
- Pneumonia and bronchiolitis; occasionally fatal
- Epidemics
- **No vaccine**
- **Antivirals are available:** ribavizine

## 4. Rhinovirus

- **Common colds**
- > 100 serotypes; no cross-immunity
- Repeated infections
- Very hard to make a vaccine

## 5. Adenovirus

- Respiratory virus
- Pharyngitis and conjunctivitis; pneumonia in young children
- Children most commonly infected
- Asymptomatic infection common
- **Vaccines used in army**

## 6. Enteric Viruses

- Enterovirus = enteric virus
- Infect intestinal/lymphoid cells
- **Poliovirus, coxsackievirus, echovirus**

- Multiply in GI tract, but RARELY cause gastroenteritis
- **Like to be in GI tract but cause problems because they go elsewhere**
- Infection via respiratory or GI tract
- Spread to other target organs in body
- 95% inapparent infection, 4-5% minor illness, 1% serious illness

### 6.1. Poliovirus

- Humans are the ONLY natural host
- Types 1, 2 and 3
- **Causes poliomyelitis**
  - Highly infectious, invades the host nervous system and can cause total paralysis in as little as a few hours
  - **Causes central nervous system clinical manifestation**
- Global Polio Eradication Initiative
  - Launched in 1988 by WHO, goal was to eliminate poliovirus in the same manner as smallpox was eliminated
  - Since 1988, number of cases has decreased by ~ 99%
  - Currently polio is only found in parts of Africa and South Asia
- Diagnosis
  - **Isolation** from stool samples (5-6 weeks after infection), CSF and pericardial fluid
  - **Serology:** acute and convalescent phases
  - \*\*\* carriers with inapparent infection are able to spread the disease to susceptible individuals\*\*\*
  - Some people are asymptomatic
- Prevention
  - **Vaccination:**
    - Salk vaccine (Jonas Salk)
      - Killed/inactivated vaccine; does not produce local immunity in GI of host; virus can still colonize host GI tract and SPREAD to community
      - Used for immunocompromised
    - Sabin vaccine (most common; Albert Sabin)
      - Live attenuated vaccine; host will produce IgA and IgG, so its protected against intestinal colonization and virus can NOT replicate and spread
      - Oral admission

### 6.2. Coxsackieviruses

- Groups A and B
- Seasonal variation
- Diagnosis by stool sample and paired sera (same as polio)
- **Causes**
  - aseptic meningitis- take CSF and rule out bacteria, parasites and fungi,
  - Herpangina- often seen as cankers, warts, etc
  - Pleurodynia- infects intercostal muscles, mistaken for heart attacks

- **NO VACCINE**

### 6.3. Echoviruses

- Several types
- **Enteric Cytopathogenic Human Orphan Viruses**
- Minor respiratory illness
- Aseptic meningitis
- Same diagnosis as coxsackie and polioviruses
- **NO VACCINE**

## 7. Viruses of Diarrhea

- **7.1 ROTAVIRUS**
  - Epidemics in infants; mainly in winter
  - **Children form 0-17**
  - Replication in small intestine
  - Acute gastroenteritis → vomiting, diarrhea, fever
  - Highly infectious
  - Diagnosis:
    - EM or immunological testing of virus from stool samples
  - Epidemiology
    - Short incubation
    - Fecal-oral route, aerosols, fomites
    - Outbreaks in daycare centres, children's hospitals
  - Prevention:
    - Rapid diagnosis and isolation of patient
    - Proper handwashing
    - **Vaccine available**
- **7.2 NOROVIRUS**
  - Outbreaks of gastroenteritis in older children and adults (**ages 18+**)
  - Diagnosis:
    - First exclude bacterial cause, then can be differentiated from bacterial gastroenteritis
  - Epidemiology:
    - **VERY CONTAGIOUS; survives well on objects/environment**
      - Fecal-oral route; food-borne outbreaks, often found on **crew ships** lol
  - Prevention:
    - **No vaccine**; handwashing and isolation of infected individuals
- **7.3 ADENOVIRUSES** (also a respiratory virus) \*DON'T NEED TO KNOW THESE 2\*
  - Some types cause gastroenteritis in children
  - Can NOT cultivate diarrhea type in cell culture
  - Diagnosis by EM
- **7.4 CALICI- and ASTRO- VIRUSES**
  - Sporadic gastroenteritis in children

- EM diagnosis
- Fecal-oral route of transmission

## 8. Viruses Causing Rashes

- Common epidemiological features of viruses causing rashes:
  - Humans are the only reservoir
  - Highly contagious!
- Measles, Rubella (German measles), Varicella (chicken pox), Herpes simplex (HSV), Papilloma virus

### 8.1 Measles

- One of the **highest infectivity rates**
- Clinical:
  - rash first appears behind ears, forehead and nostrils then spreads to whole body; **BLOTCHY appearance**
  - **Usually red and raised and then will turn brown**
- Lifelong immunity after natural infection
- Complications:
  - secondary bacterial infections; ex. Bronchopneumonia
    - Encephalitis (rare)
    - Exacerbation of TB and leukemia
  - **Koplik spots will appear before the rashes**
- Diagnosis:
  - Serological
  - Confirmation of suspected case:
    - IgM Ab in single blood specimen against measles or a rising
    - IgG Ab titer against measles in paired blood
  - Immune status
    - Circulating measles specific Ab IgG
- Prevention
  - **Immunoglobulin:** can suppress disease if given within 5 days of contact with virus
  - **Live attenuated vaccine:** very effective, widely used, given after 12 months of age

### 8.2 Rubella (German Measles; 3-day measles)

- **Very dangerous for non-immune pregnant women** → birth defects
- Largest danger is in first trimester
  - 50% chance of damage to the fetus
- **Flat and pink rash DOES NOT turn brown**
- Birth defects:
  - General: abortion, death of newborn
  - Localized: cataracts, deafness, heart defects
  - Other: low birth weight, cleft palate, mental deficiency
- Clinical:

- Similar to measles but milder; life long immunity
- Epidemiology and Immunity:
  - Pre-vaccine era, seen in school children during winter and spring, outbreaks every 7-10 years, leads to life long immunity
- Lab diagnosis
  - Suspected cases: detection of rubella specific IgM or rising Ab titer in paired sera
  - Immunity status: detection of circulating Rubella Ab (IgG)
- Prevention of congenital rubella:
  - Check immune status of women who could/want to be pregnant
  - Diagnosis in hospitals
  - Rubella serology screening of men and women starting work in hospitals
  - Vaccination of non-immune
  - Isolation of rubella cases in hospitals
- **Vaccination- live attenuated vaccine**
  - **DO NOT give vaccine to women who are already pregnant**

### 8.3 Varicella

- **chickenpox: Varicella Zoster Virus (VZV)**
- Clinical
  - Childhood febrile illness with characteristic rash
    - Crops of fresh vesicles appear within 3-4 days of onset
    - In non-immune adults, occasional pneumonia, may be fatal
- Herpes Zoster (Shingles)
  - The virus from chicken pox stays in your central nervous system. It comes out one of your nerves in a strip and therefore causes shingles
  - Limited rash, along trajectory of one nerve
  - Late recurrence of latent VZV infection
- Diagnosis:
  - ID of virus particles in pustules by EM or immuno methods, followed by cell culture
- Prevention:
  - **Vaccine**; detection of susceptible persons by serological methods

### 8.4 Herpes Simplex Virus (HSV)

- Widespread
- Become LATENT after initial infection; lesions appear periodically
- High percentage of inapparent infections
- Epidemiology:
  - **HSV1: cold sores**- oral and ocular lesions; transmitted via oral and respiratory secretions
  - **HSV2: herpes genitalis**- associated with genital tract; infected females can transmit to newborns
- Diagnosis: ID of virus particles by EM or immuno methods; cell cultures; serology NOT useful
- Clinical forms (other than cold sores):
  - Genital infections: recurrent in both sexes

- Herpetic encephalitis: RARE
- Neonatal Herpes: acquired during birth from asymptomatic mother; difficult to prevent; can result in death or severe sequelae
- Herpetic Whitlow: affects fingers, occupational hazard of health care workers; nosocomial infections in neonates
- Corneal and Conjunctival Infection: can cause ulceration of cornea and blindness
- Treatment and Prevention:
  - Antivirals; C-section for symptomatic mothers; vaccines coming soon

## 8.5 Papilloma Viruses

- **Cause different types of warts**
  - Common warts on hands and feet
  - Genital warts: sexual transmission, asymptomatic carriers
  - Some types associated with cancer: cervix, vulva, penis
- Diagnosis:
  - Immuno techniques and DNA hybridization techniques; no cell cultures available
- Prevention:
  - **Vaccine now available (Gardasil)**
    - Gardasil used to be for women to get vaccinated before they were sexually active
    - Everyone is encouraged to get it