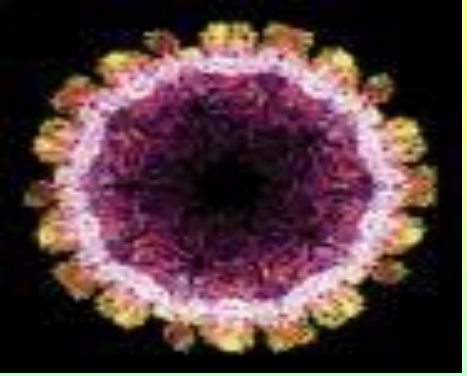
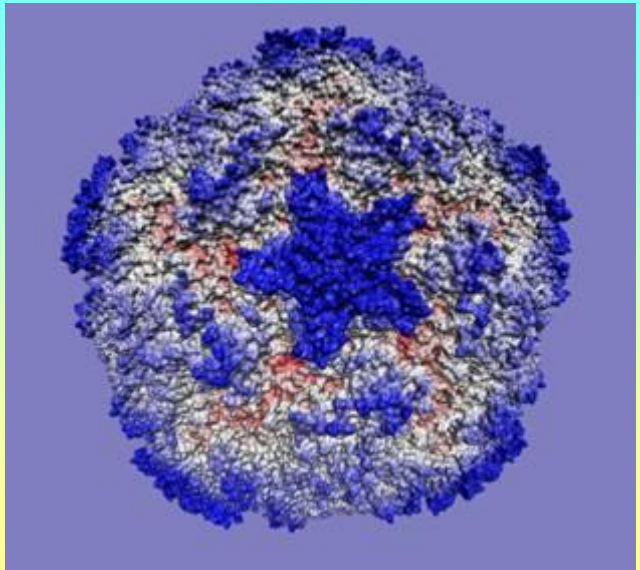
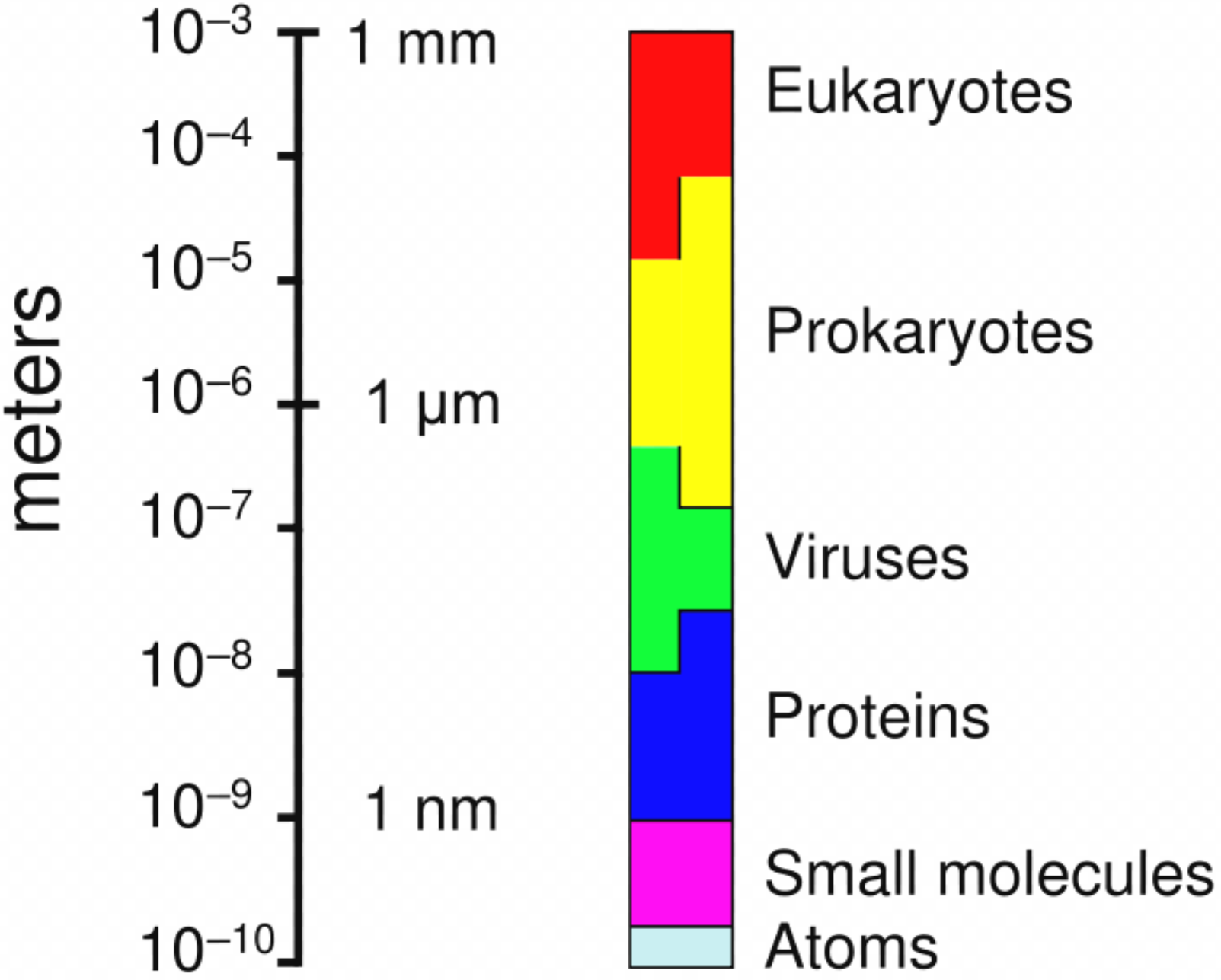


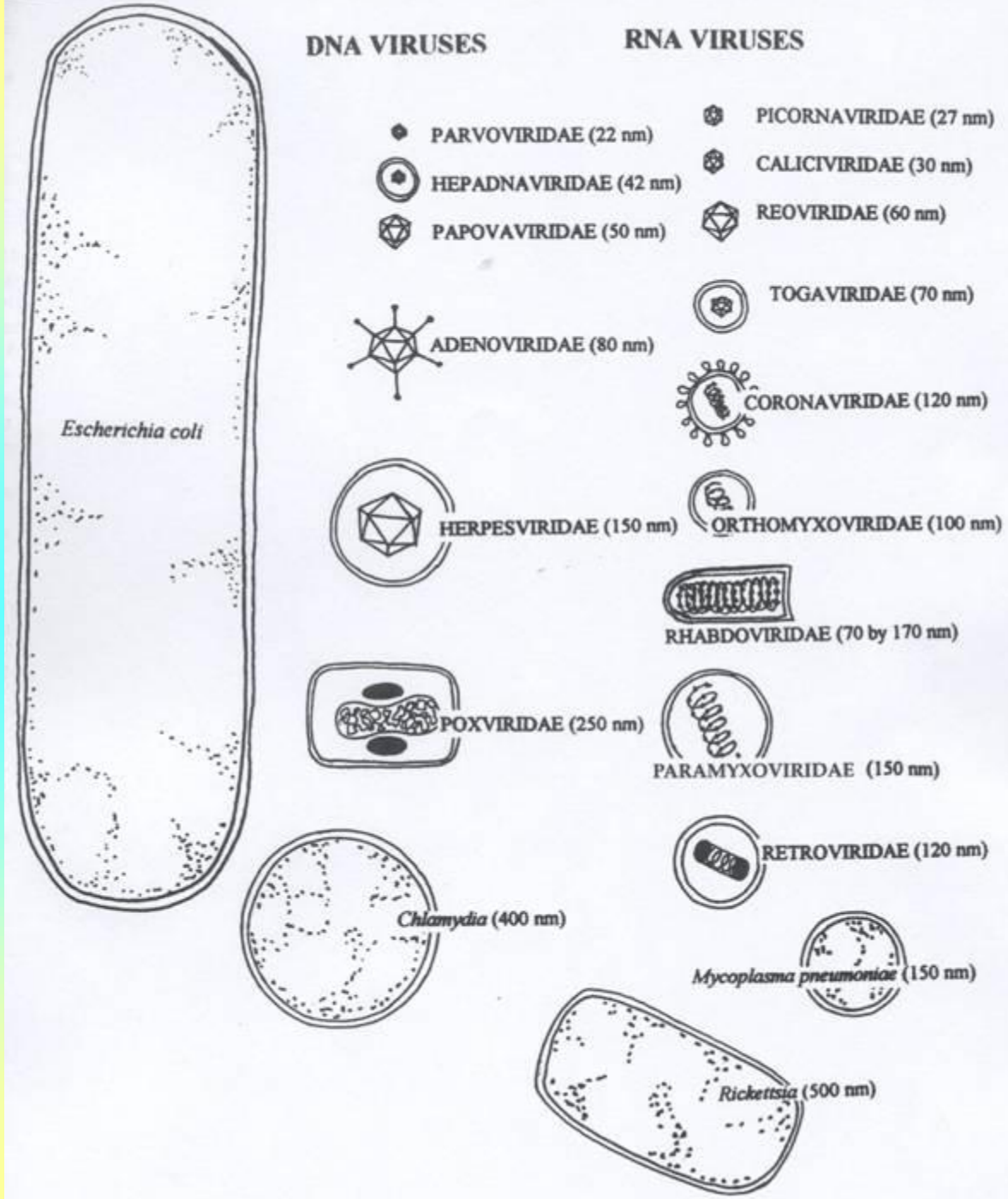
VIRUSES

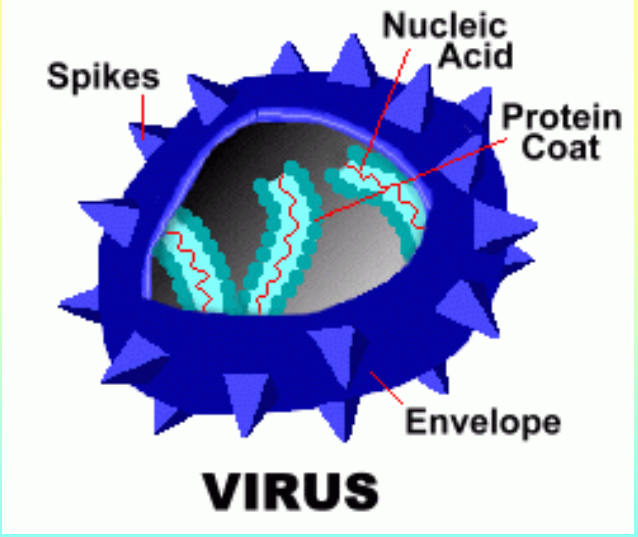


General Characteristics

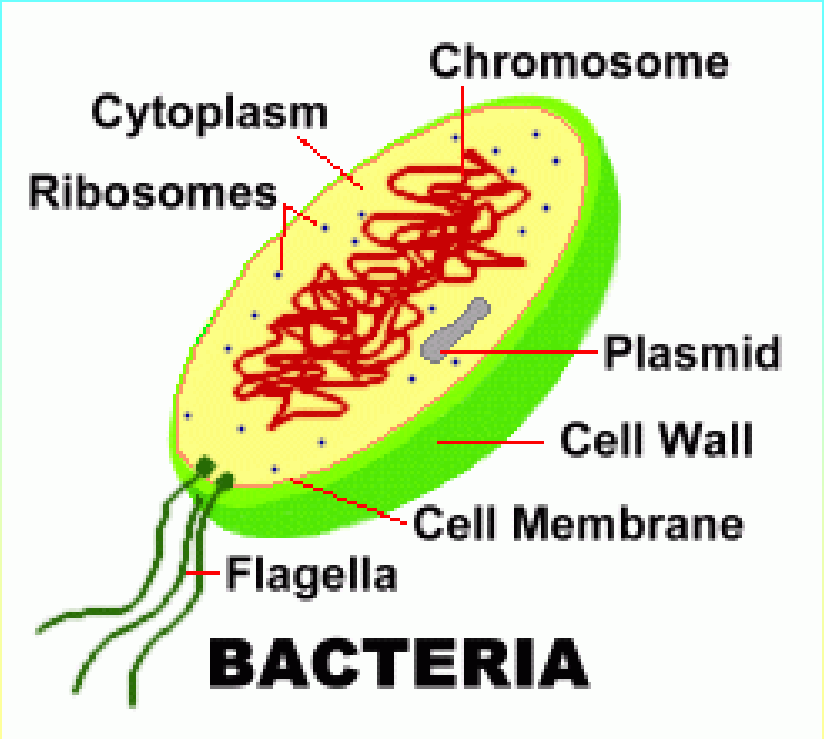
- Require LIVING cells for growth and replication (cell cultures, embryonated eggs, living animals/plants)
- Have DNA or RNA…NEVER both!
- Multiply by separate synthesis of nucleic acid and protein, combine to form virus particles
- Size varies from 10 nm-300 nm


meters
10^{-3}
10^{-4}
10^{-5}
10^{-6}
10^{-7}
10^{-8}
10^{-9}
10^{-10}
1 mm
1 µm
1 nm
Eukaryotes
Prokaryotes
Viruses
Proteins
Small molecules
Atoms

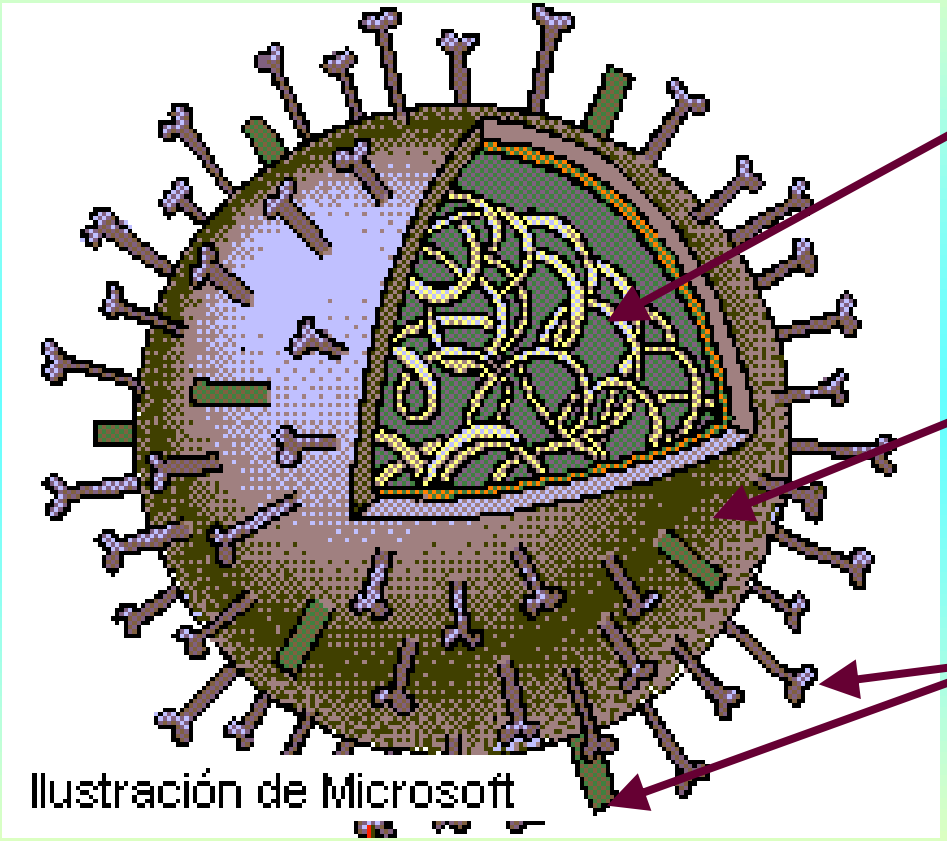

DNA VIRUSES
RNA VIRUSES
PARVOVIRIDAE (22 nm)
HEPADNAVIRIDAE (42 nm)
PAPOVAVIRIDAE (50 nm)
PICORNAVIRIDAE (27 nm)
CALICIVIRIDAE (30 nm)
REOVIRIDAE (60 nm)
TOGAVIRIDAE (70 nm)
ADENOVIRIDAE (80 nm)
CORONAVIRIDAE (120 nm)
Escherichia coli
HERPESVIRIDAE (150 nm)
ORTHOMYXOVIRIDAE (100 nm)
RHABDOVIRIDAE (70 by 170 nm)
POXVIRIDAE (250 nm)
PARAMYXOVIRIDAE (150 nm)
RETROVIRIDAE (120 nm)
Chlamydia (400 nm)
Mycoplasma pneumoniae (150 nm)
Rickettsia (500 nm)



?? What are viruses made of ??



Basic Components



Nucleic Acid

-infectious genetic material

Protein Coat

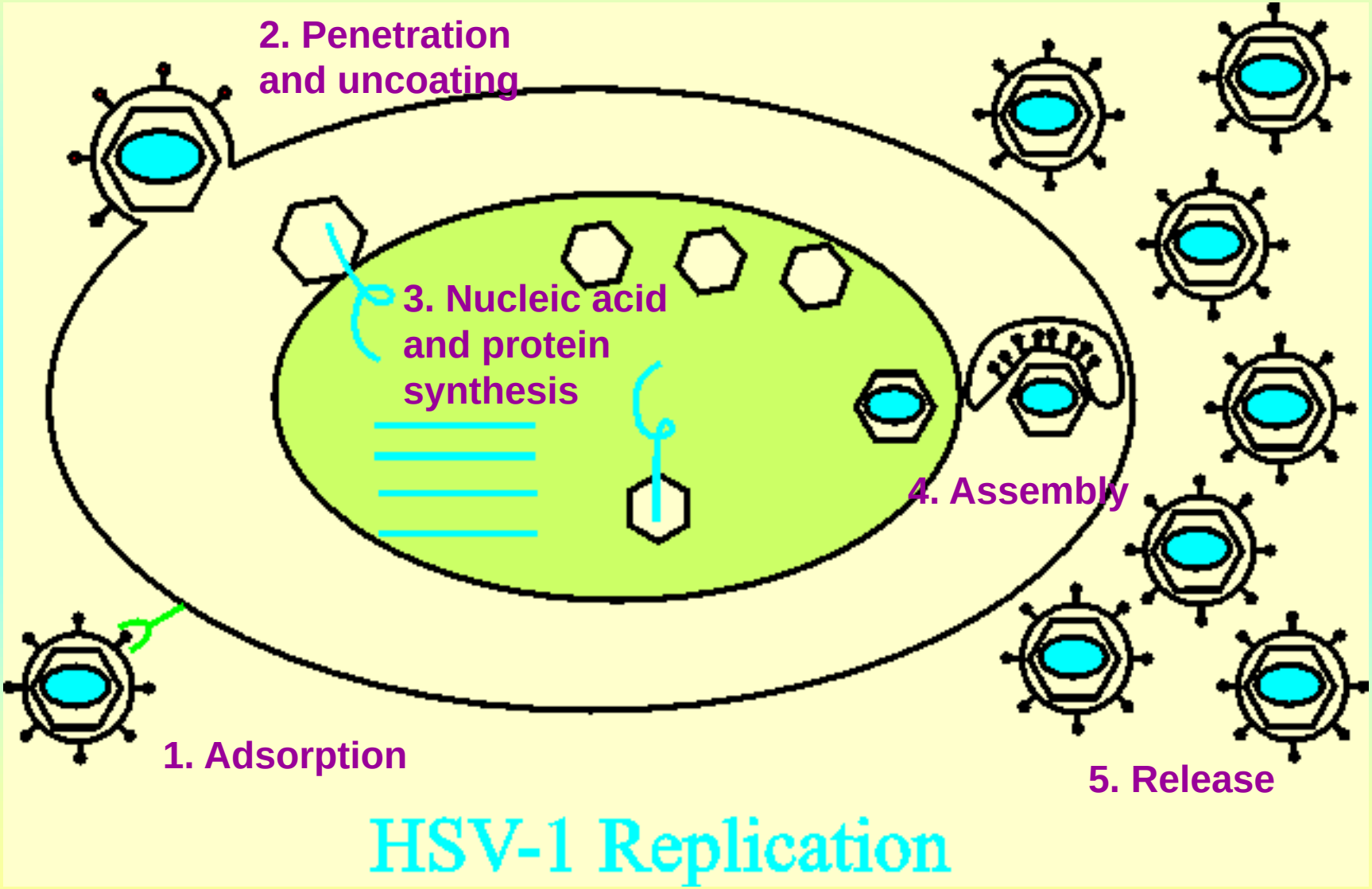
-protective

Surface Antigens

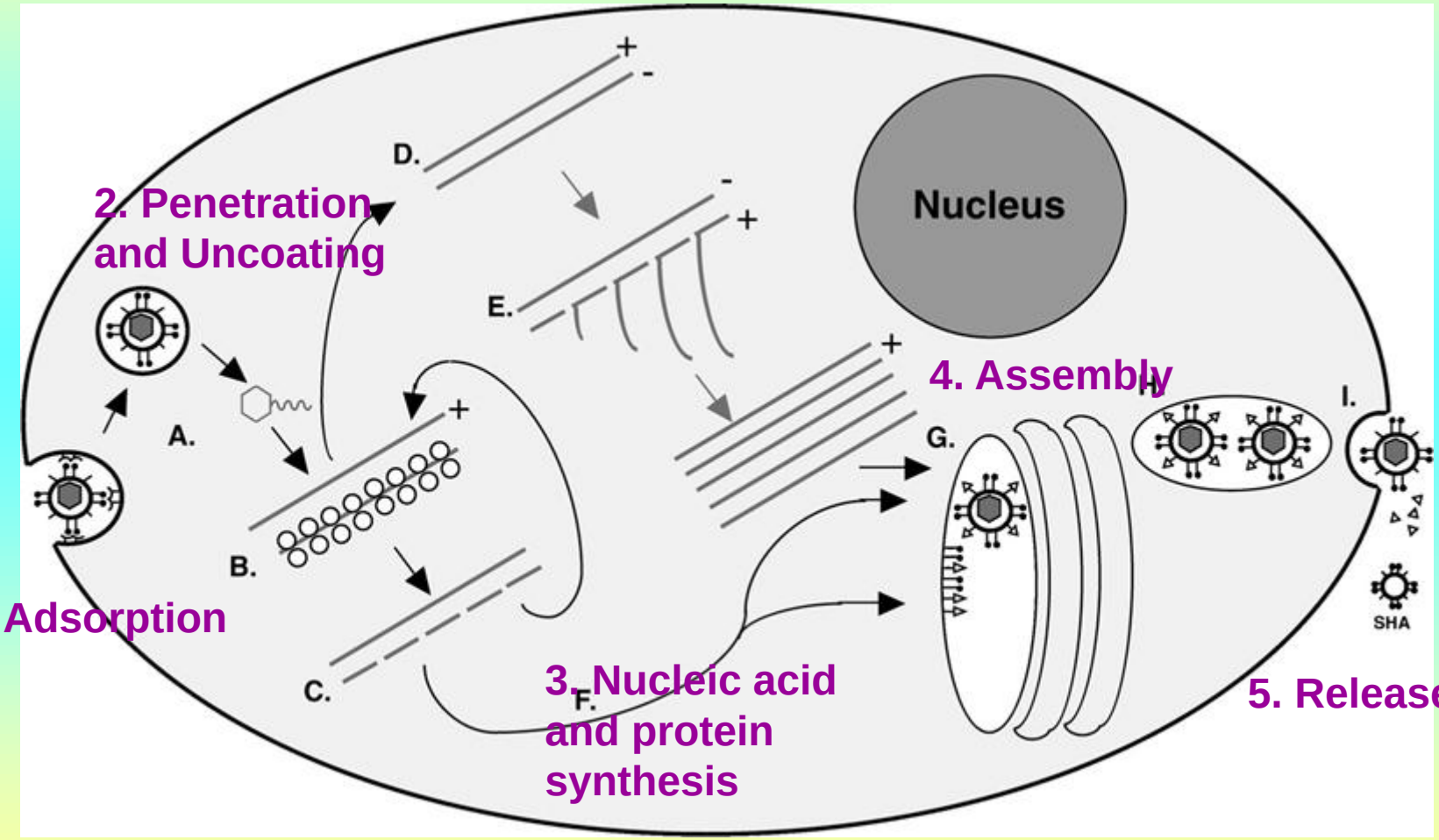
-protein or carbohydrate

-highly variable

REPLICATION



REPLICATION



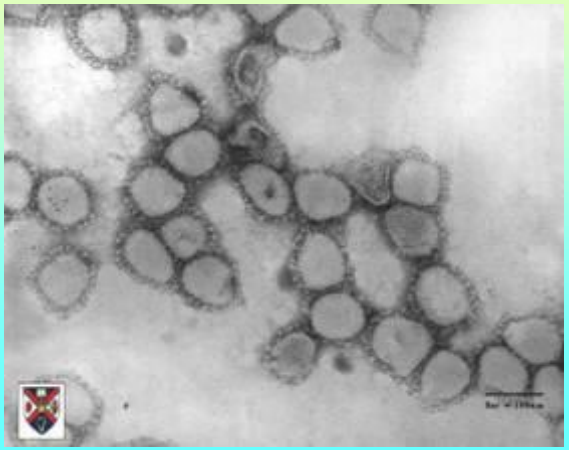
West Nile Virus Replication

How do we detect viral infections?

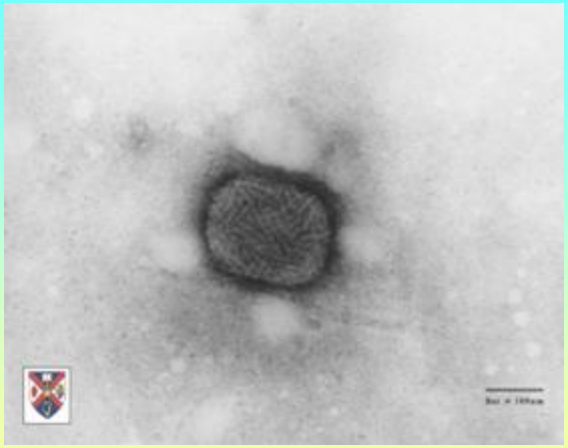
1. Detect the virus itself!
2. Detect the immune response…antibodies against the virus!

Viral Diagnosis

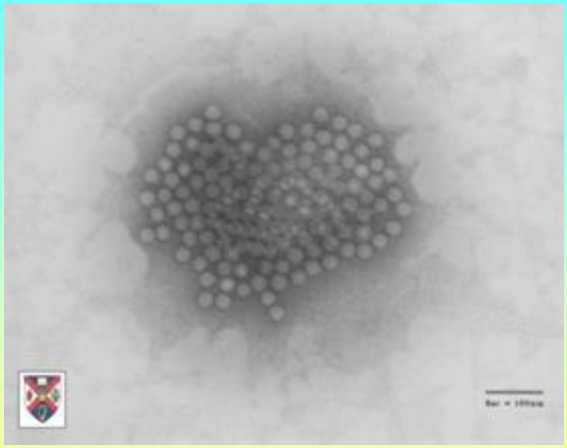
- **A. Detection in clinical specimens**
  - **1. Visualisation by Electron microscopy**



EM Coronaviridae

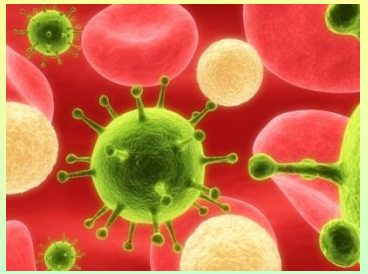


EM Poxviridae

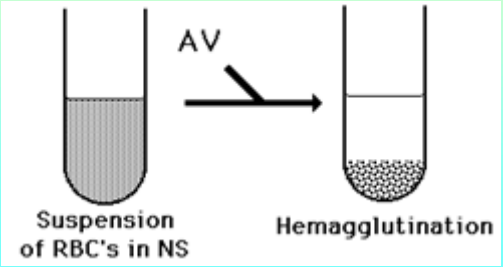


EM Picornaviridae

Viral Diagnosis



- **A. Detection in clinical specimens**
  - **2. Cell culture (cytopathic effects, hemagglutination, immunofluorescence)**



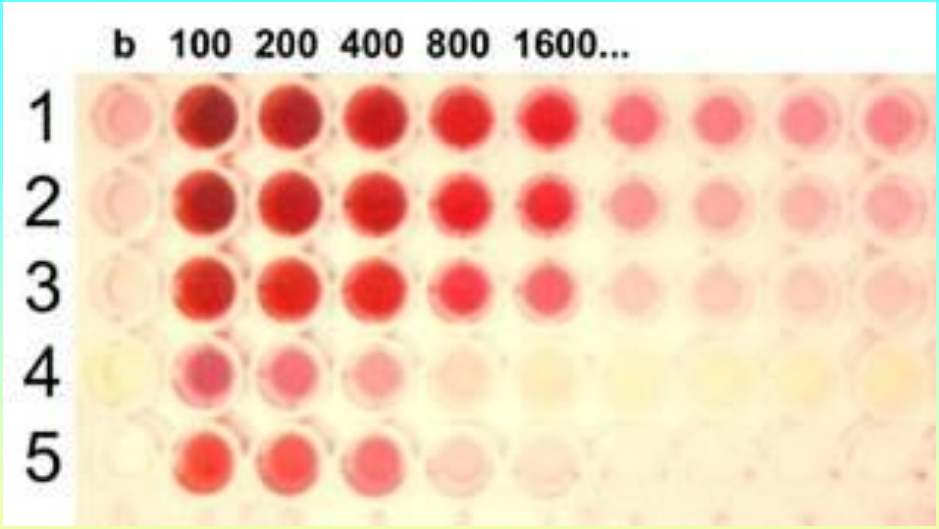
Adenovirus induces hemagglutination

Cytopathic effect of herpes simplex virus

Immunofluorescence of hepatitis C in cell culture

Viral Diagnosis

- **B. Detection of patient's immune responses**
  - Antibody detection, presence or absence (ELISA)
    - IMMUNITY TEST
  - Rise in antibody titre or high antibody titre
    - DIAGNOSTIC TEST



Determine titre

What types of viruses will we learn about?

1. Viruses of the breathing
2. Enteric viruses
3. Viruses of diarrhea
4. Viruses of the rashes

Next week…

1. Viruses of the glands
2. Viruses of the liver
3. Viruses of the brain
4. Viruses of the immune system…aka…HIV

Respiratory Viruses

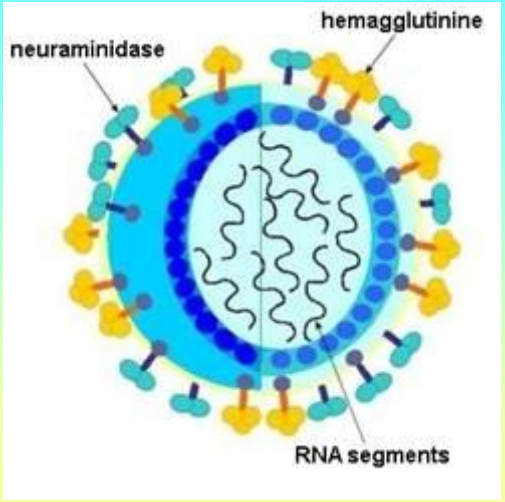
- Respiratory disease
- Different families
  1. Influenza viruses
  2. Parainfluenza viruses
  3. Respiratory syncytial viruses
  4. Rhinoviruses
  5. Adenoviruses
  6. Echoviruses, coxsackie viruses, herpes viruses (occasional respiratory tract infection)

Influenza Viruses

- Influenza virus type A: major epidemics
- Influenza virus type B: milder disease

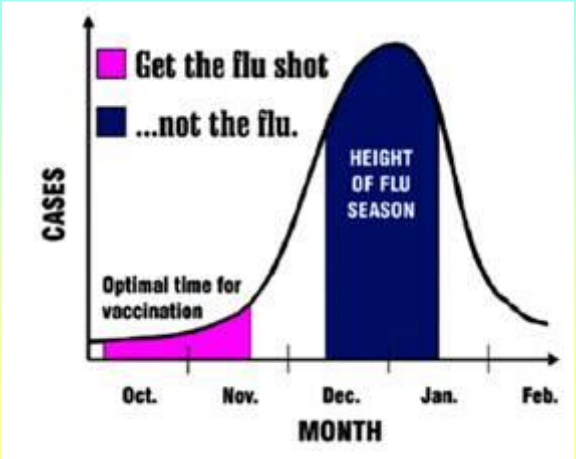
- Produce haemagglutinin (diagnostic)

- Frequent recombination
  = High antigenic variability
  = Pandemics



Influenza Viruses

- Clinical:
  - fever, variable respiratory symptoms
  - Infants and elderly more susceptible
- Diagnosis:
  - Throat washings, naso-pharyngeal aspirate inoculated into cell culture
- Serum:
  - Paired sera (acute and convalescent stage)
- Prevention:
  - Annual vaccination
    especially for high risk groups



This year it's a different flu season.

World Health Organization

25 April 2009 : Pandemic phase 3. Surveillance for flu should be intensified

27 April 2009 : Pandemic phase 4. The likelihood of a pandemic has increased

29 April 2009 : Pandemic phase 5. Countries activate pandemic plans

11 June 2009 : Pandemic phase 6. Worldwide influenza pandemic

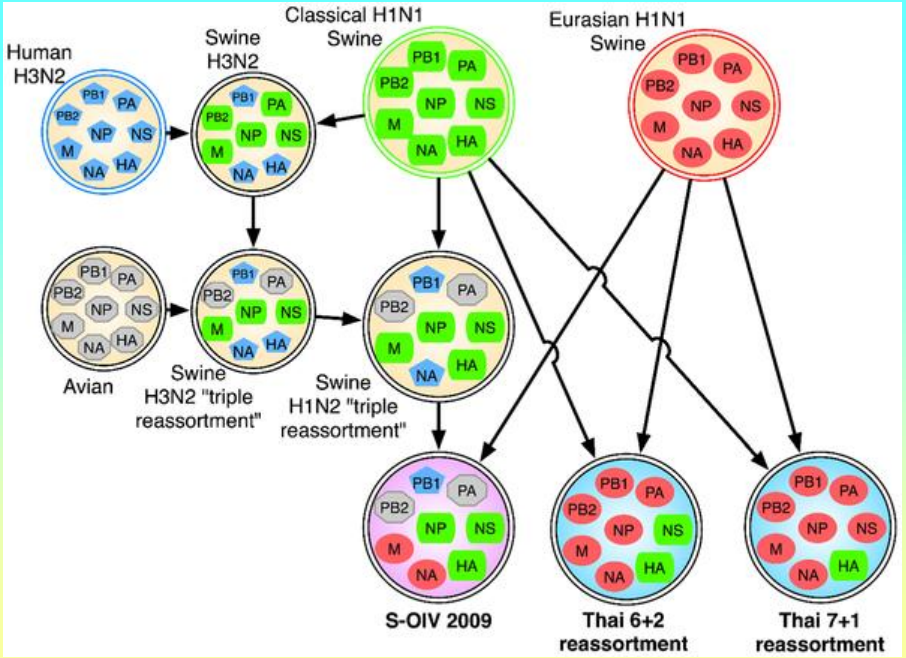
The WHO Pandemic response and planning is a direct reflection of disease SPREAD and not of disease SEVERITY

What about disease severity?

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

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. unadjuvanted 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

Parainfluenza viruses

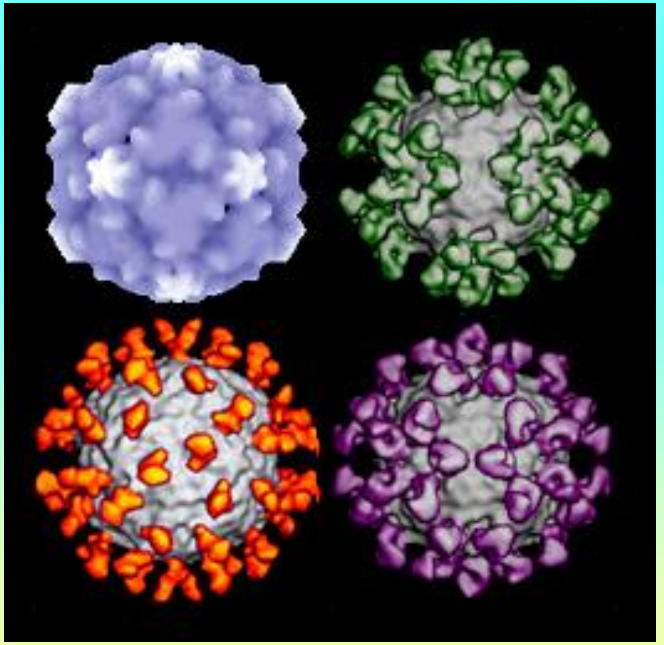
- Infants and young children
- Respiratory infection that could have serious complications
- Croup (barking cough, high pitch sound on inhalation)
- Bronchiolitis, bronchopneumonia
- No vaccine

Respiratory syncytial virus

- Major respiratory pathogen for children < 2years
- Pneumonia and bronchiolitis; occasionally fatal
- Epidemics
- No vaccine
- Antiviral: Ribavizine

Rhinovirus

- Common colds
- > 100 serotypes; no cross-immunity
- Repeated infections



http://www.ncbi.nlm.nih.gov/ICTVdb/WIntkey/Images/3d_hrv14.jpg

Flu vs. Colds: A Guide to Symptoms

Questions	Flu	Cold
Was your child's onset of illness ...	sudden?	slow?
Does your child have a ...	high fever?	no (or mild) fever?
Is your child's exhaustion level ...	severe?	mild?
Is your child's head ...	achy?	headache-free?
Is your child's appetite ...	decreased?	normal?
Are your child's muscles ...	achy?	fine?
Does your child have ...	chills?	no chills?

Symptoms	Cold	Flu
Fever	Rare	Usual; high (100°F to 102°F; occasionally higher, especially in young children); lasts 3 to 4 days
Headache	Rare	Common
General Aches, Pains	Slight	Usual; often severe
Fatigue, Weakness	Sometimes	Usual; can last up to 2 to 3 weeks
Extreme Exhaustion	Never	Usual; at the beginning of the illness
Stuffy Nose	Common	Sometimes
Sneezing	Usual	Sometimes
Sore Throat	Common	Sometimes
Chest Discomfort, Cough	Mild to moderate; hacking cough	Common; can become severe
Treatment	Antihistamines Decongestant Nonsteroidal anti-inflammatory medicines	Antiviral medicines—see your doctor
Prevention	Wash your hands often Avoid close contact with anyone with a cold	Annual vaccination; antiviral medicines—see your doctor
Complications	Sinus congestion Middle ear infection Asthma	Bronchitis, pneumonia; can be life threatening

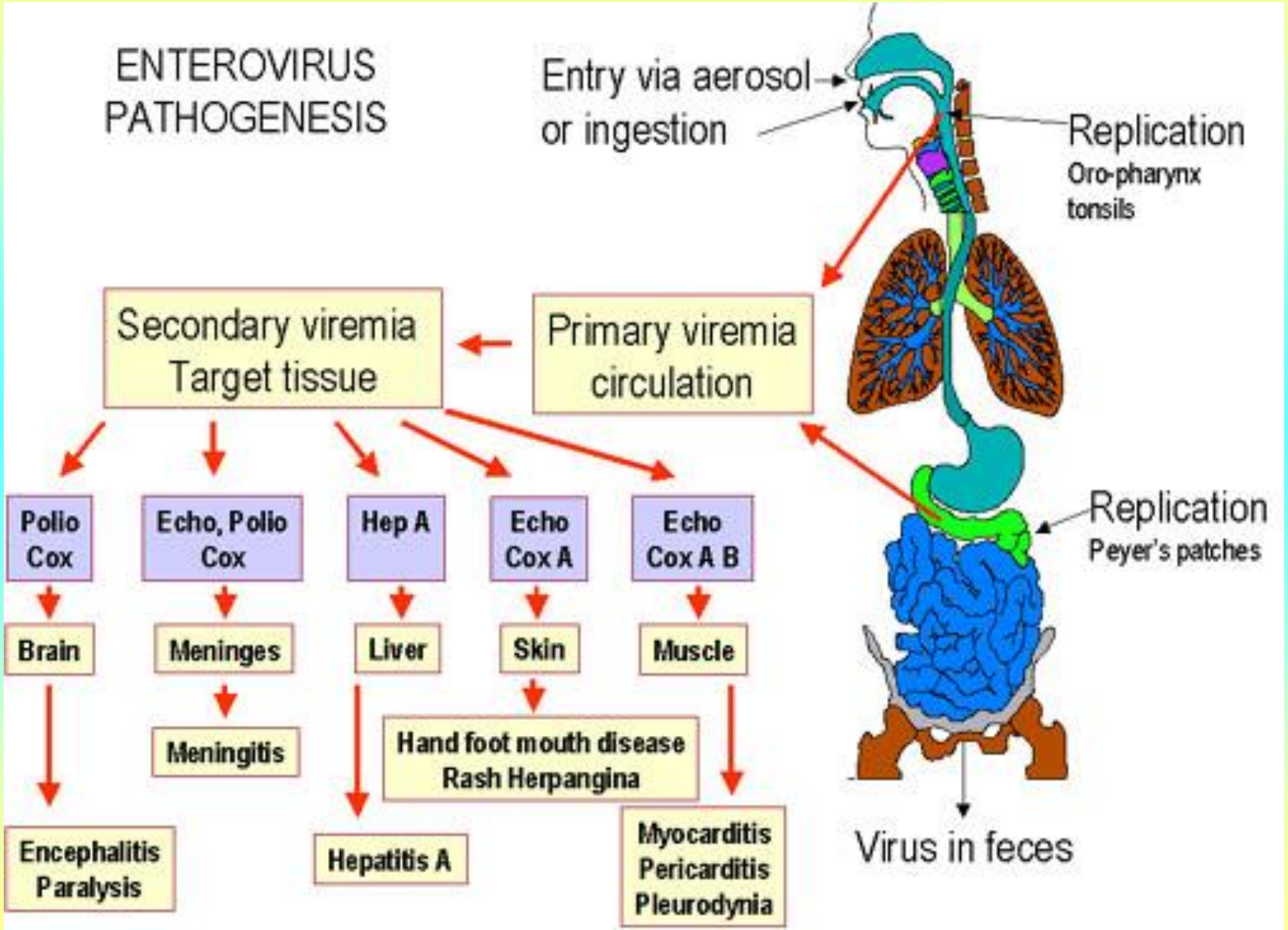
Adenovirus

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

ENTERIC VIRUSES

- Enterovirus = Enteric virus
- Infect intestinal / lymphoid cells
- Poliovirus, coxsackievirus, echovirus
- Multiply in GI tract, but RARELY cause gastro-enteritis
- Infection via respiratory or GI tract
- Spread to other target organs in body
- 95% inapparent infection, 4-5% minor illness, 1% serious illness

Enteroviruses



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
- 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% (from > 350,000 cases in 1988 to 1997 cases in 2005)
  - Currently polio is only found in parts of Africa and South Asia (Nigeria, India, Pakistan, Afghanistan)

http://www.who.int/mediacentre/factsheets/fs114/en/

Poliovirus Diagnosis

- Isolation from stool samples (up to 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*

Polio Prevention

- **VACCINATION**
  - **Salk vaccine (Jonas Salk)**
    - Killed/inactivated vaccine; does not produce local immunity in GI of host (IgA); Virus can still colonize host GI tract and SPREAD to the community!!!
    - used for immunocompromised
  - **Sabin vaccine (most common; Albert Sabin)**
    - Live attenuated; host will produce IgA and IgG, so is protected against intestinal colonization and virus can NOT replicate and spread
    - Oral administration

Coxsackieviruses

- Groups A and B
- Seasonal variation
- Diagnosis by stool sample and paired sera (same as polio)
- NO VACCINE

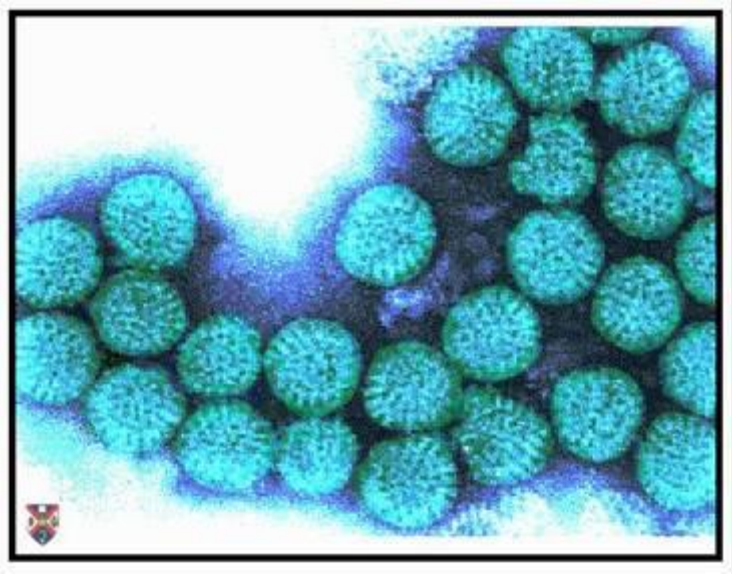
	Group A	Group B
Minor Respiratory Illness		√
Aseptic Meningitis	√	√
Herpangina and hand-foot-and-mouth disease	√	
Pleurodynia, pericarditis and myocarditis		√

Echoviruses

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

Viruses of Diarrhea

- ROTAVIRUS
  - Epidemics in infants (6 months-2yrs); mainly in winter
  - Replication in small intestine
  - Acute gastroenteritis ⟶ vomiting, diarrhea, fever
  - Highly infectious!!!

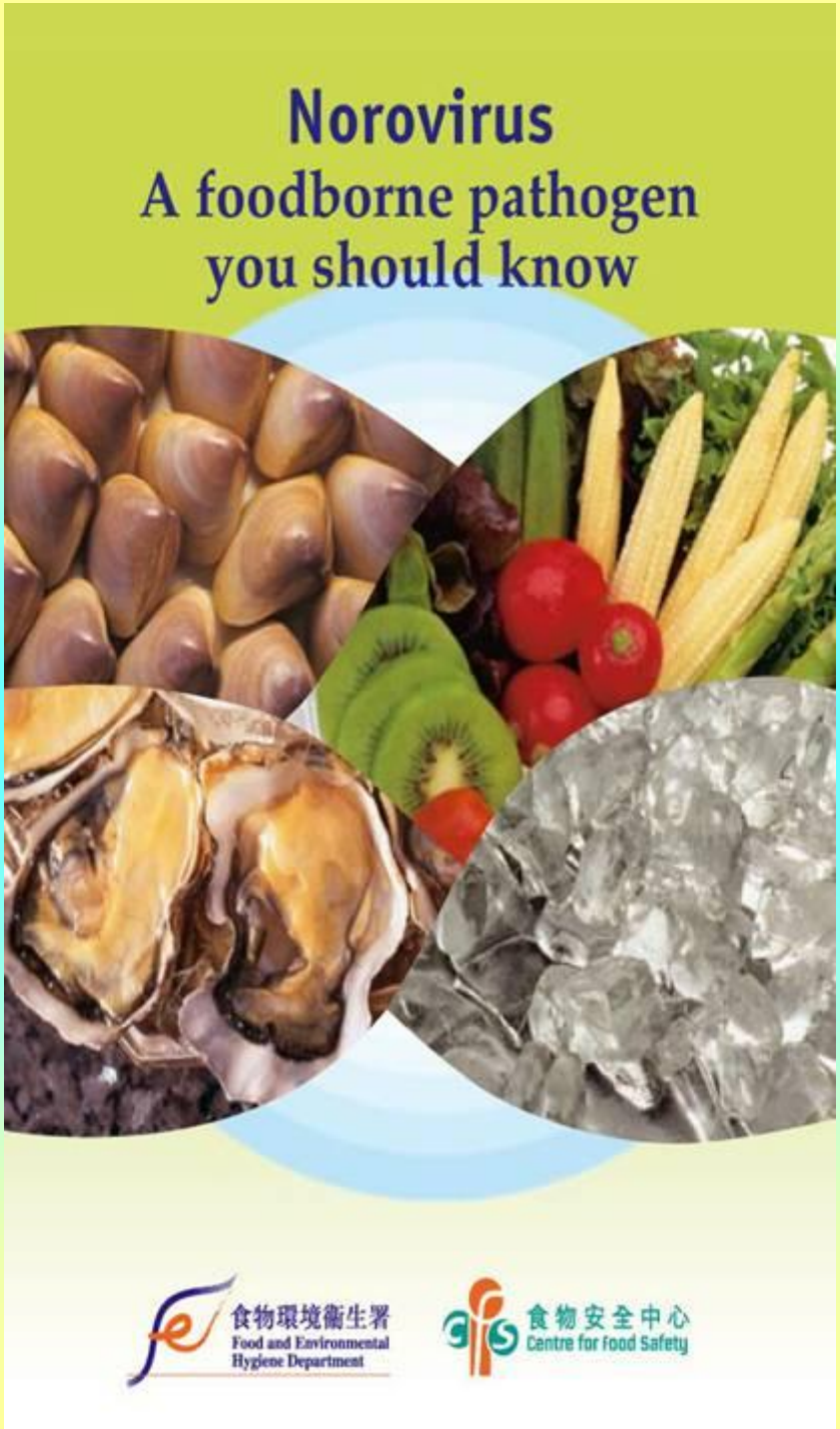


Rotavirus

- Diagnosis
  - EM or immunological testing of virus from stool samples (within 3 days)
- Epidemiology
  - Short incubation (2-3days)
  - Fecal-oral route, aerosols (explosive diarrhea), fomites
  - Outbreaks in daycare centres, children's hospitals
- Prevention
  - Rapid diagnosis and isolation of patient
  - Proper handwashing
  - To vaccinate or not to vaccinate?

Norovirus

- Outbreaks of gastroenteritis in older children and adults
- 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
- Prevention: no vaccine; handwashing and isolation of infected individuals



- US CDC estimated in 1999 (Mead et al.) that of all foodborne illness:
  - ✓ 30% is bacterial
  - ✓ 3% is parasitic
  - ✓ **67% is viral**
- Of viral foodborne outbreaks:
  - ✓ More than 90% attributed to Noroviruses
- Lopman et al. (2003) estimated in Europe the proportion is >85% of the non-bacterial foodborne illnesses attributable to norovirus
- In the Netherlands, it is estimated to be at least 54%

Other Diarrheal Viruses

- Adenoviruses (also a respiratory virus!)
  - Some types cause gastroenteritis in children
  - Can NOT cultivate diarrhea type in cell culture
  - Diagnosis by EM
- Calici- and Astro- viruses
  - Sporadic gastroenteritis in children
  - EM diagnosis
  - Fecal-oral route of transmission

Viruses Causing Rashes

- Common epidemiological features of viruses causing rashes:
  - Humans are the only reservoir
  - Highly contagious!

Viruses Causing Rashes

- Measles
- Rubella (German measles)
- Varicella (chickenpox)
- Herpes simplex (HSV)
- Papilloma virus

Measles

- One of the highest infectivity rates
- Clinical: rash first appears behind ears, forehead and nostrils then spreads to whole body; BLOTCHY appearance
- Lifelong immunity after natural infection
- Complications: secondary bacterial infections, e.g., bronchopneumonia
  - Encephalitis (rare)
  - Exacerbation of TB and leukemia

Measles

- 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. Administer after 12 months of age
    - MMR

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 if non-immune mother is infected between 0-4 weeks
- Birth defects:
  - General: abortion, death of newborn
  - Localized: cataracts (infection during 6th week)
    deafness (infection during 9th week)
    heart defects (infection during 5th-10th week)

  Other: low birth weight, cleft palate, mental deficiency

Rubella

- Clinical: similar to measles but milder; life-long immunity
- Epidemiology and Immunity: pre-vaccine era, seen in school children during winter in spring, outbreaks every 7-10 years, lead to life-long immunity
  - Now most cases (60%) are seen in those 15 years and older

Rubella

- Lab Diagnosis:
  - Suspected cases: detection of rubella specific IgM or rising Ab titer in paired sera
  - Immunity status: detection of circulating Rubella Ab (IgG)

Rubella

- Prevention of congenital rubella:
  - Check immune status of women of childbearing age
  - 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!

Varicella

- Chickenpox: Varicella Zoster Virus (VZV)
- Clinical: childhood febrile illness with characteristic rash
  - Successive crops of fresh vesicles appear within 3-4 days of onset
  - In non-immune adults, occasional pneumonia, may be fatal

Varicella

- Herpes Zoster (Shingles)
  - LIMITED rash, along trajectory of ONE nerve
  - Late recurrence of latent VZV (chicken pox) infection
- Diagnosis: ID of virus particles in pustules by EM or immuno methods, followed by cell culture
- Prevention: no vaccine?; detection of susceptible persons by serological methods

Herpes Simplex Virus (HSV)

- Widespread
- Become LATENT after initial infection; lesions reappear 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 the newborn
- Diagnosis: ID of virus particles by EM or immuno methods; cell cultures; Serology NOT useful

HSV

- Clinical forms (other than cold sores):
  - Genital infections: recurrent in both sexes
  - Herpetic encephalitis: RARE (see CNS viruses)
  - Neonatal Herpes: acquired during birth from asymptomatic mother; difficult to prevent; can result in death or severe sequelae (see CNS viruses)
  - 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; NO VACCINE

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)