Basic Epidemiological Concepts and Terms

- Incidence: # of new cases of disease/total # at risk.
- Incidence rate: Incidence/unit of time.
  - Cumulative Incidence: Incidence measured over longer period

- Prevalence: # cases (or # with defined condition) existing at specific time.
- Prevalence rate: # of such cases/total # at risk.

- P = I X D, where D is duration

Basic Epidemiological Concepts and Terms

- **Risk**- The number of individuals who are exposed and become ill divided by the number of those exposed

- **Relative Risk**- The risk of illness for individuals exposed divided by the risk of illness for those not exposed

Example

	# Ill that did eat	Total # eating	# Ill that did not eat	Total # not Eating
Quiche	2	10	3	5
Cheesecake	4	5	1	10
Swiss Roll	3	7	2	8
Chocolate Cake	1	3	4	12
Cheese Dip	4	11	1	4

What Are Relative Risks for Each Food Item???

Food	Relative Risk
Quiche	0.33
Cheesecake	8
Swiss Roll	1.72
Chocolate Cake	0.93
Cheese Dip	1.44

Basic Epidemiological Concepts and Terms

- **Odds for Cases**- Number of cases exposed to a factor divided by the number of cases not exposed to the factor
- **Odds for Controls**- Number of controls exposed to a factor divided by the number of controls not exposed to the factor
- **Odds Ratio**- Odds for cases divided by odds for controls
  - **$OR = O_{cases}/O_{controls}$**

Example

	Cases	Controls
Exposed	a	b
Not Exposed	c	d

What is Odds Ratio???

OR = (a/c)/(b/d) = ad/bc

Koch's Postulates

- Organism must be consistently present in diseased state
- Organism must be isolatable and culturable
- Cultured organism must induce disease when introduced to susceptible host

Basic Epidemiological Concepts and Terms

- Confounding- when a factor is associated with the exposure one is studying and which at the same time is associated with the outcome

- Causation- nine criteria outlined by Sir Austin Bradford Hill in 1965.
  - **Strength** (is the risk so large that we can easily rule out other factors)
  - Consistency (have the results have been replicated by different researchers and under different conditions)
  - Specificity (is the exposure associated with a very specific disease as opposed to a wide range of diseases)
  - **Temporality** (did the exposure precede the disease)
  - **Biological gradient** (are increasing exposures associated with increasing risks of disease)
  - **Plausibility** (is there a credible scientific mechanism that can explain the association)
  - Coherence (is the association consistent with the natural history of the disease)
  - Experimental evidence (does a physical intervention show results consistent with the association)
  - Analogy (is there a similar result that we can draw a relationship to)

Dynamic Population Model

- SIR Model (n = S + I + R)
  - S= Susceptibles
  - I= Infectious
  - R=Resistants

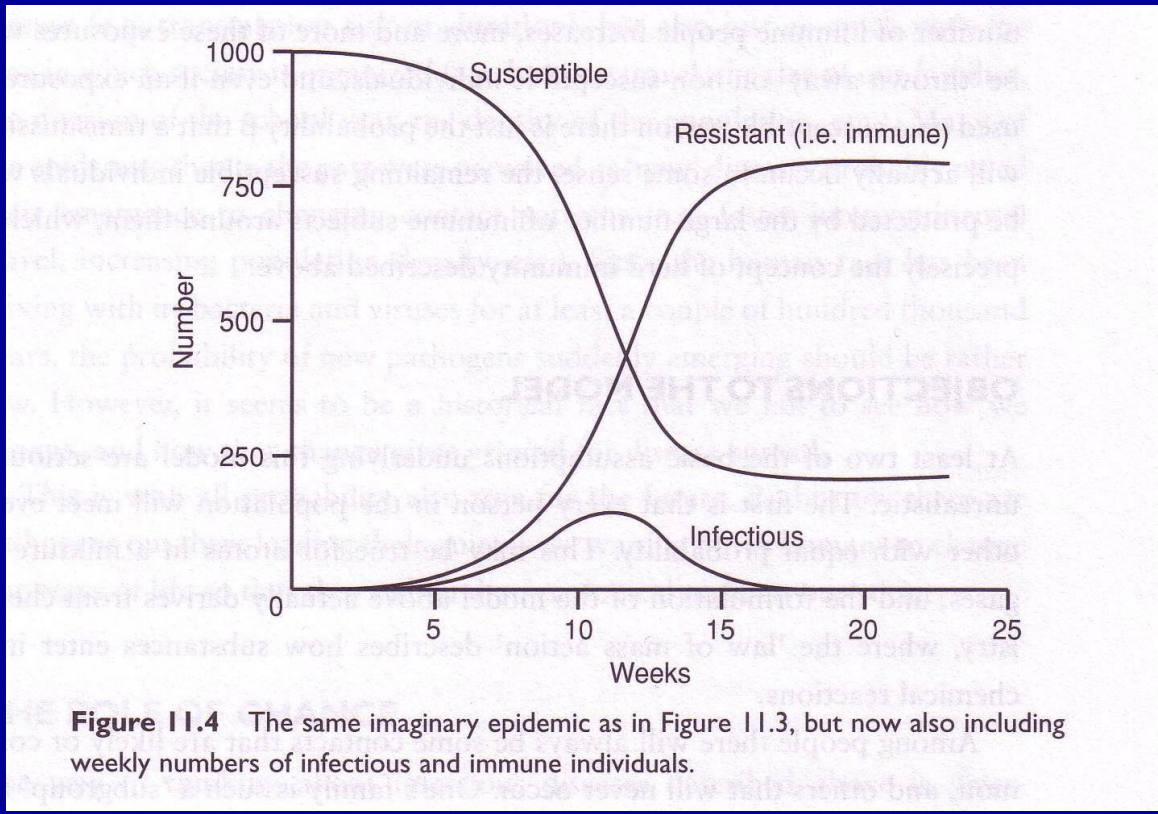


Figure 11.4 The same imaginary epidemic as in Figure 11.3, but now also including weekly numbers of infectious and immune individuals.

Viruses

What is a virus?

"**Virus**" is from the Greek meaning for "**poison**" and was initially described by Edward Jenner in 1796.

Viruses

- smallest (0.02-0.3 micrometers diameter)
- simplest (nucleic acid + protein coat (+ lipoprotein envelope))
- spherical (icosahedral) or rod-shaped (helical)
- no biological activity outside of host cells/or host organisms
  - obligate intracellular parasites; recruit host cell to make new viruses, often destroying the cell
- non-enveloped viruses are most persistent in the environment
  - protein coat confers stability
- enteric and respiratory viruses are most important for environmental health
  - transmitted by direct and indirect contact, fecally contaminated water, food, fomites and air.

Recognition of viruses

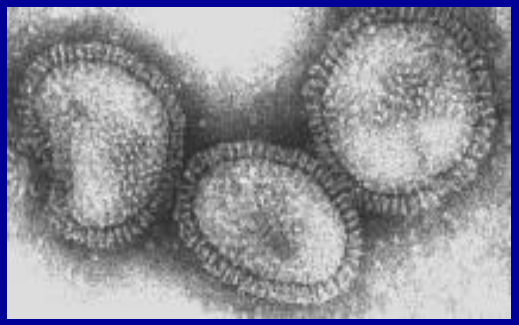
☞ **How long viruses have been within our midst?**

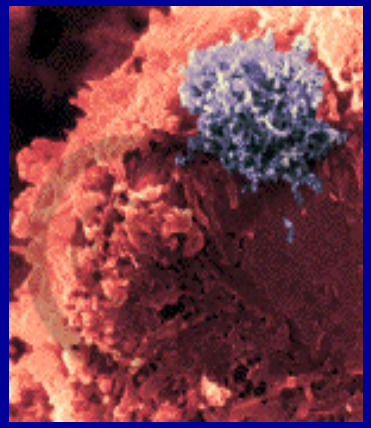
1500 BC: Leg deformities indicative of poliomyelitis, pock marks indicative of smallpox.

During the 1800's, **all infectious agents were considered to be viruses** until **Koch** developed pure culture techniques which allowed the separation and growth of bacteria. **In the late 1800's:** Bacteria were purified and established as disease causing agents. It then became possible to distinguish them from the "**filterable agents**", those able to pass through special filters designed to prevent the passage of bacteria. The first viruses described were foot and mouth disease (a picornavirus), 1898, Yellow fever (a flavivirus), 1900, Rous sarcoma virus (an oncogenic retrovirus), 1906.

Viral diseases have played a major role in human history over whatever time scale we choose to explore:

Over the past 1000 years: Smallpox and measles were brought to North and South America by early European explorers/conquerers. These diseases, for which the native American populations had no acquired partial immunity, killed large fractions of the populations, and were a major factor in the decimation of these societies.

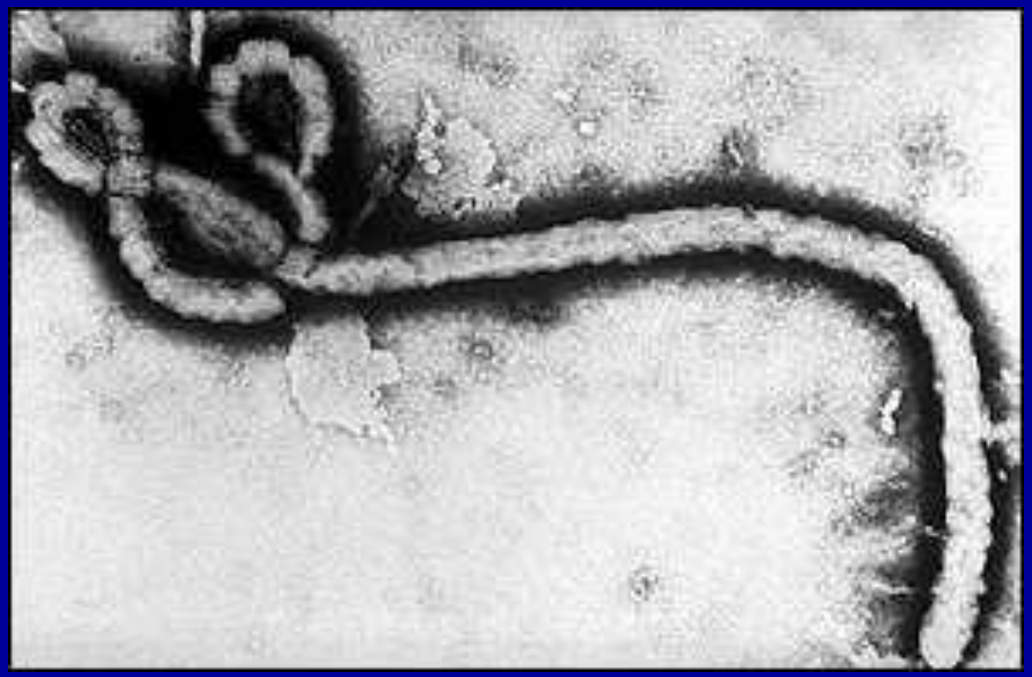




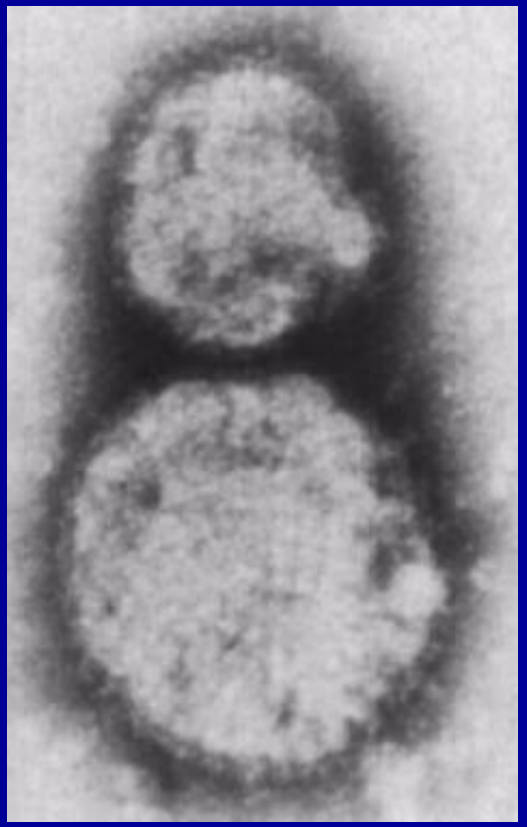
Over the past 100 years: A newly emerged strain of influenza killed 20 million people in 1918-1919 in the immediate aftermath of World War I. A decade later, polio became one of the most feared infections of children and young adults (including Franklin D. Roosevelt, the U.S. President throughout the Depression and World War II).

As the 20th century entered its final 20 years, a new ~100% lethal virus, HIV, spread rapidly around the world via body fluid transmission.

Over the past 10 years: As the global HIV epidemic continues, sporadic cases and outbreaks in humans of some non-human host viruses such as Ebola and Hanta raise the concern about future epidemics by other viruses in the new century.



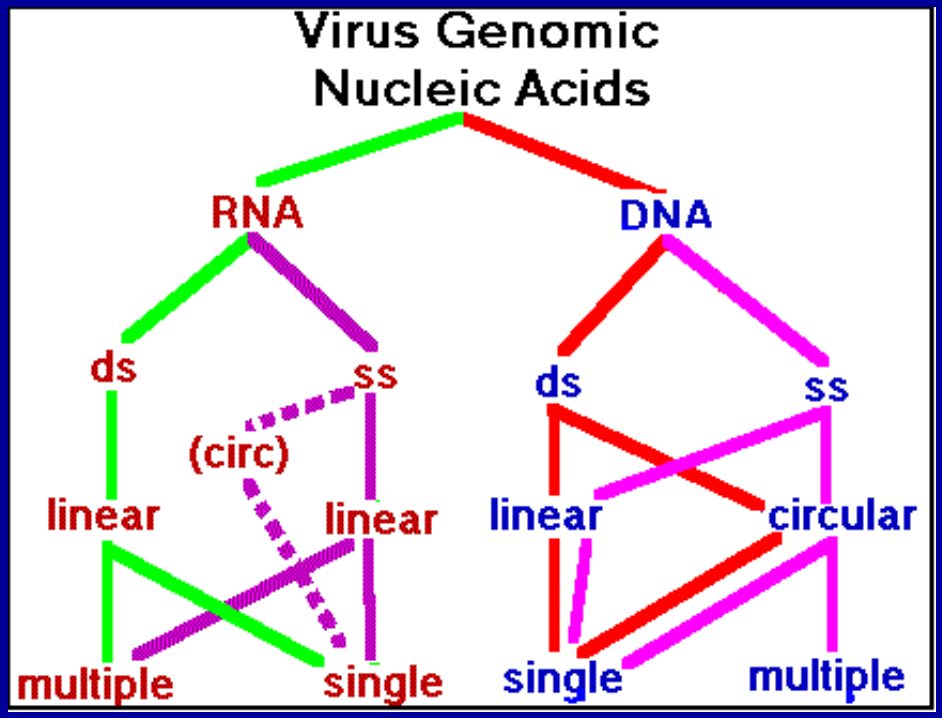
Ebola virus



Four Corners Virus
(Hanta)

Virus Composition

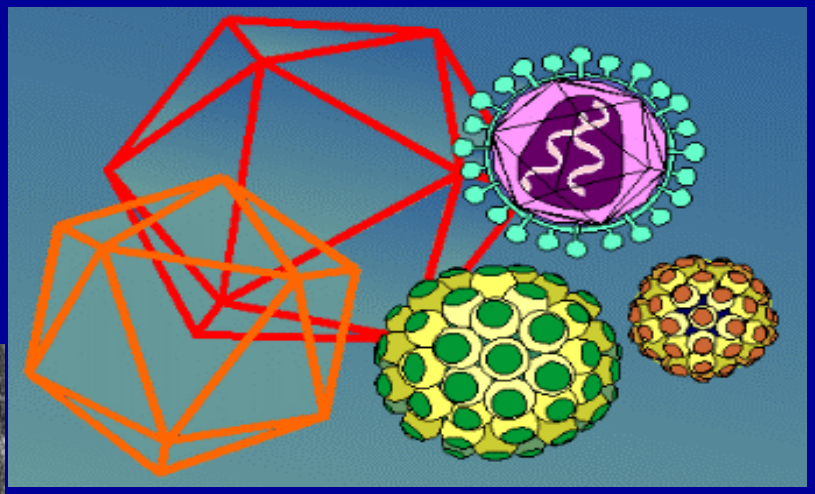
- nucleic acid:
  - RNA or DNA
  - double- or single-stranded
  - one piece or multiple, genetically distinct pieces
    - represent separate genes
    - some have multiple copies of same gene
  - linear, circular or circular+supercoiled



Virion (Viral Particle)

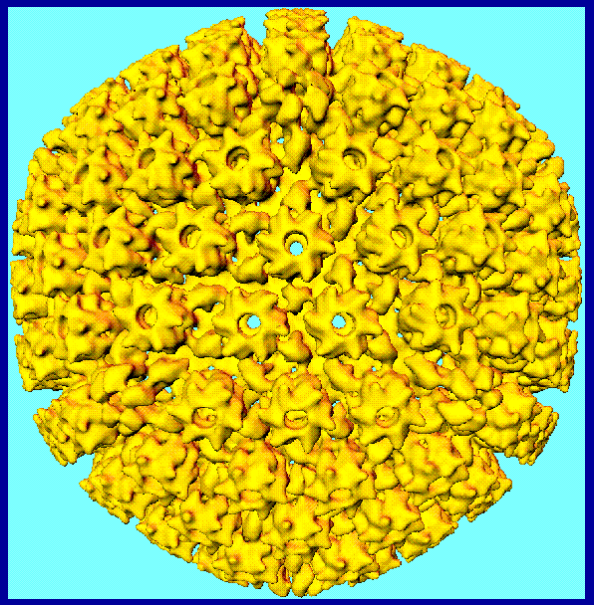
Proteins:

- Structural proteins
- Non-structural proteins

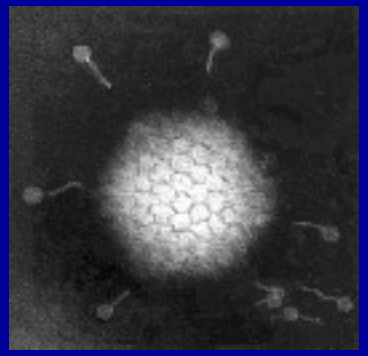


<u>Envelope:</u>

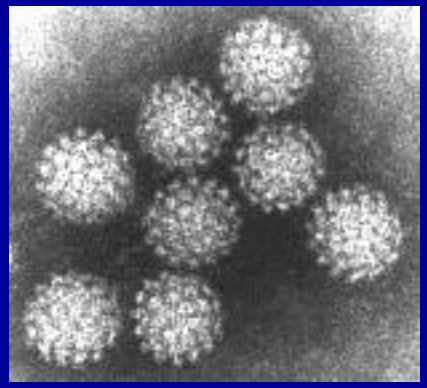
- lipid bilayer membrane + glycoproteins)
- typically acquired from host cell membranes



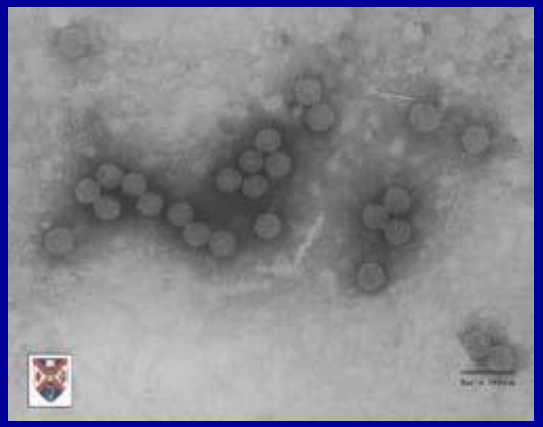
Some viral shapes



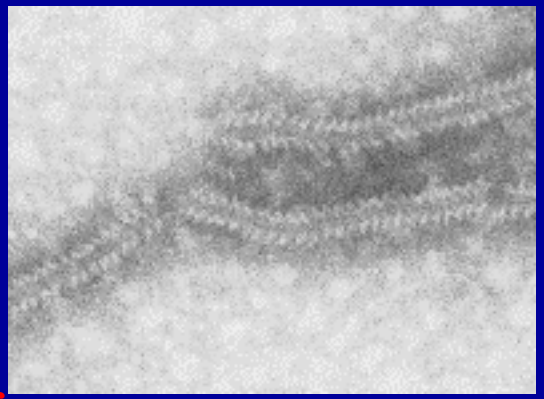
adenovirus



papillomavirus



parvovirus



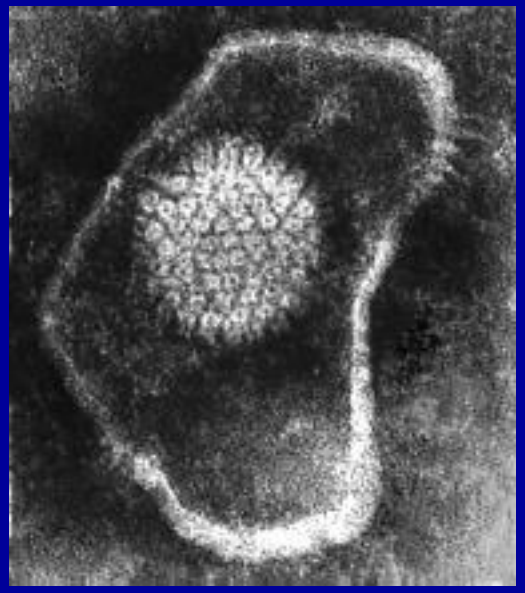
morbillivirus

100 nm

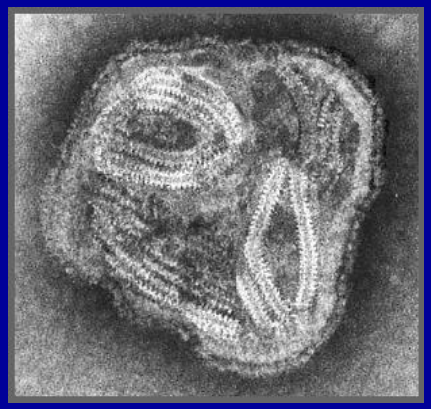
1 nm = 1 millionth of a mm
100 nm = 1 ten thousandth of a mm

Some viral shapes

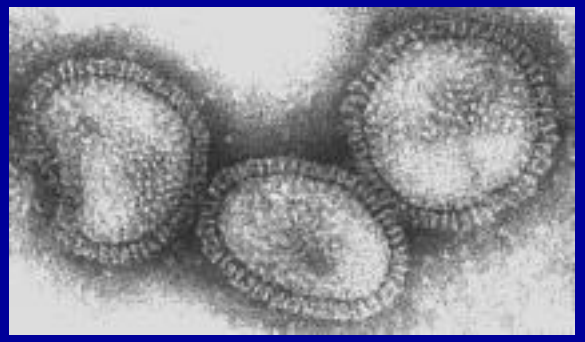
100 nm



herpesvirus



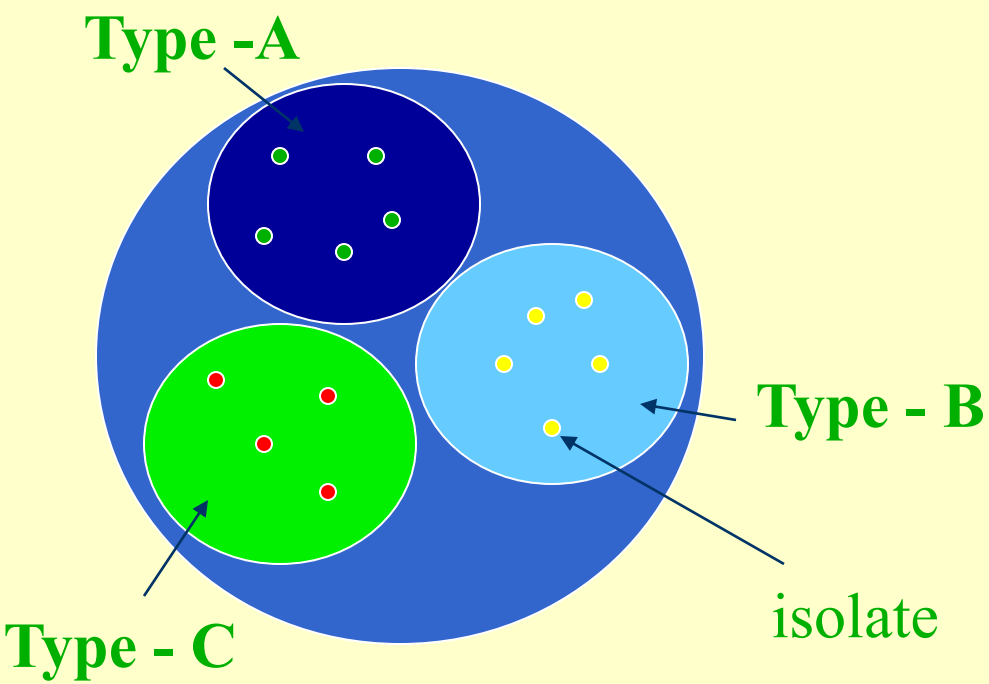
parainfluenza virus



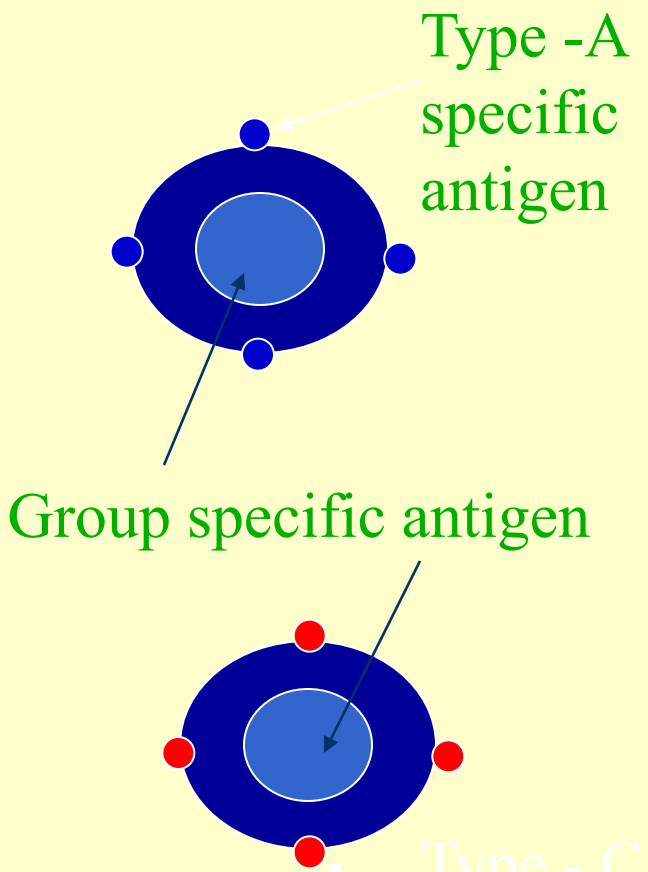
influenzavirus

poxvirus

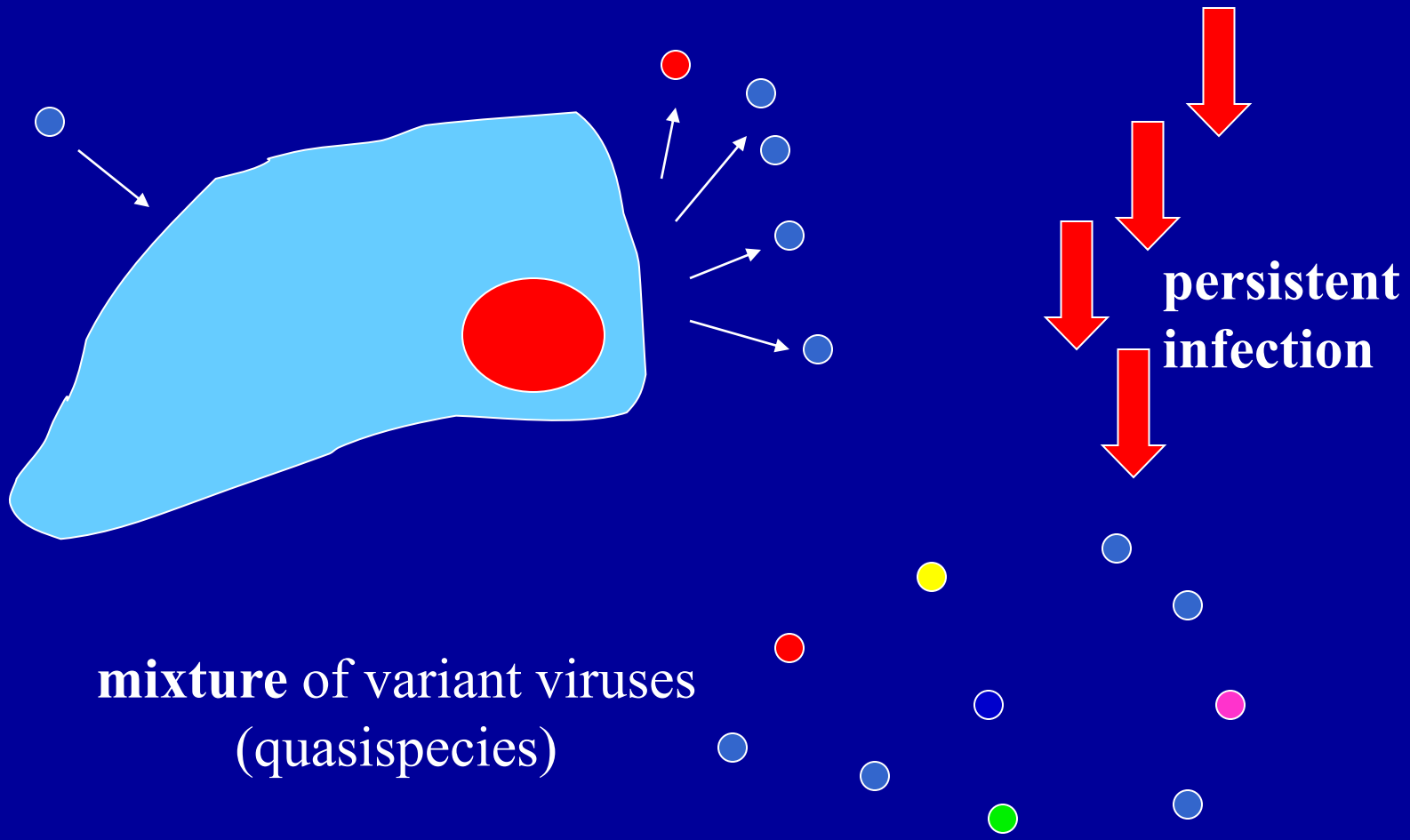
Groups, types (sero-types), isolates and 'strains'



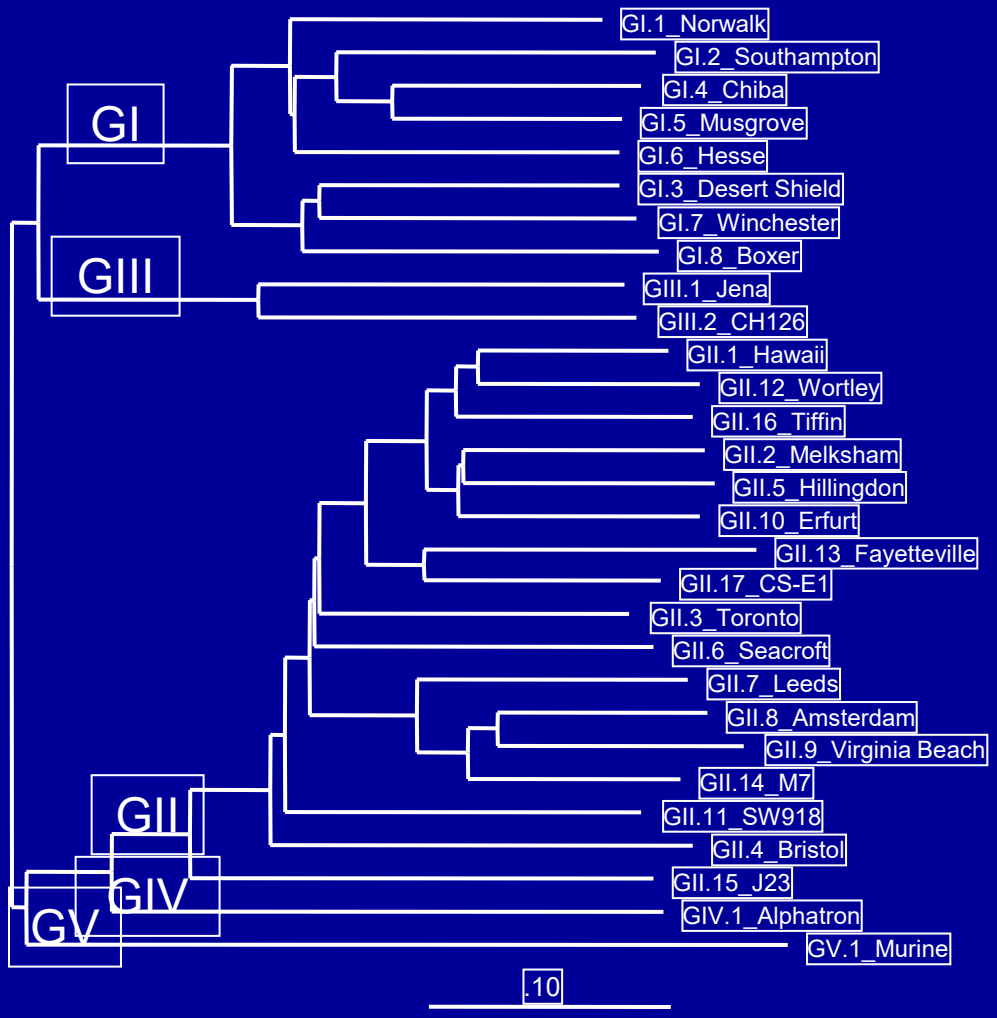
Group
(e.g.. noroviruses)



Errors in replication lead to "quasispecies"



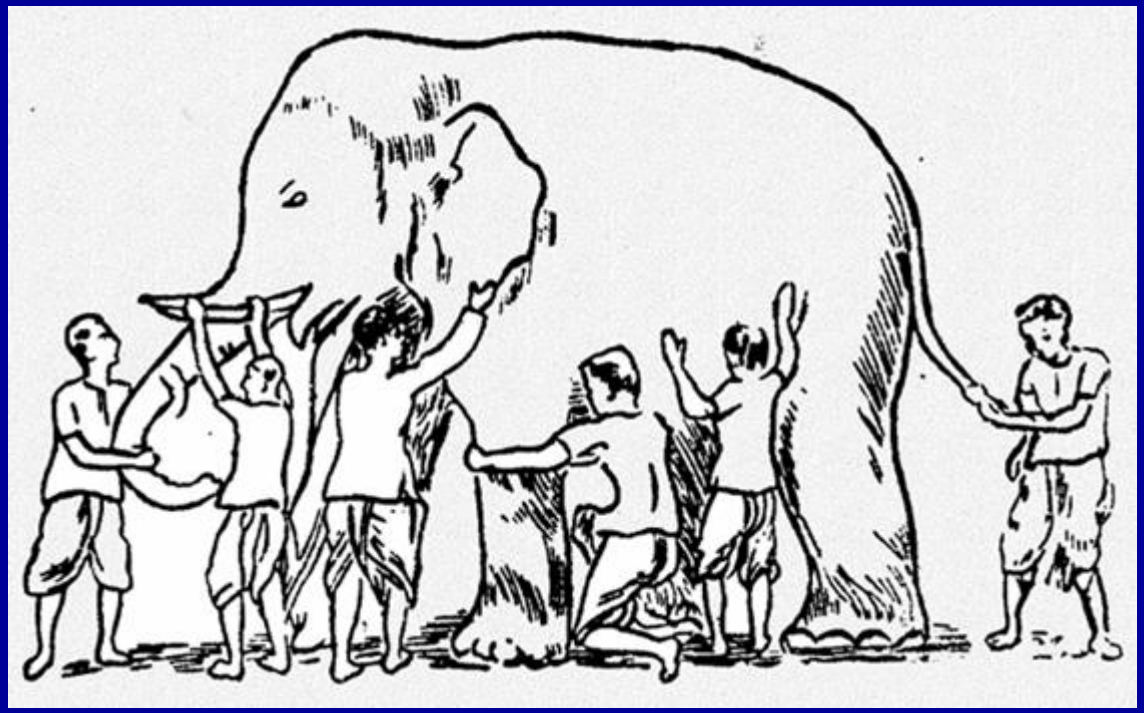
Genotypes: ex. 29 Clusters of Noroviruses



Clusters differ by ≥ 20% amino acid pairwise distance

Genogroups differ by 44-55% amino acid pairwise distance

A General Caution!

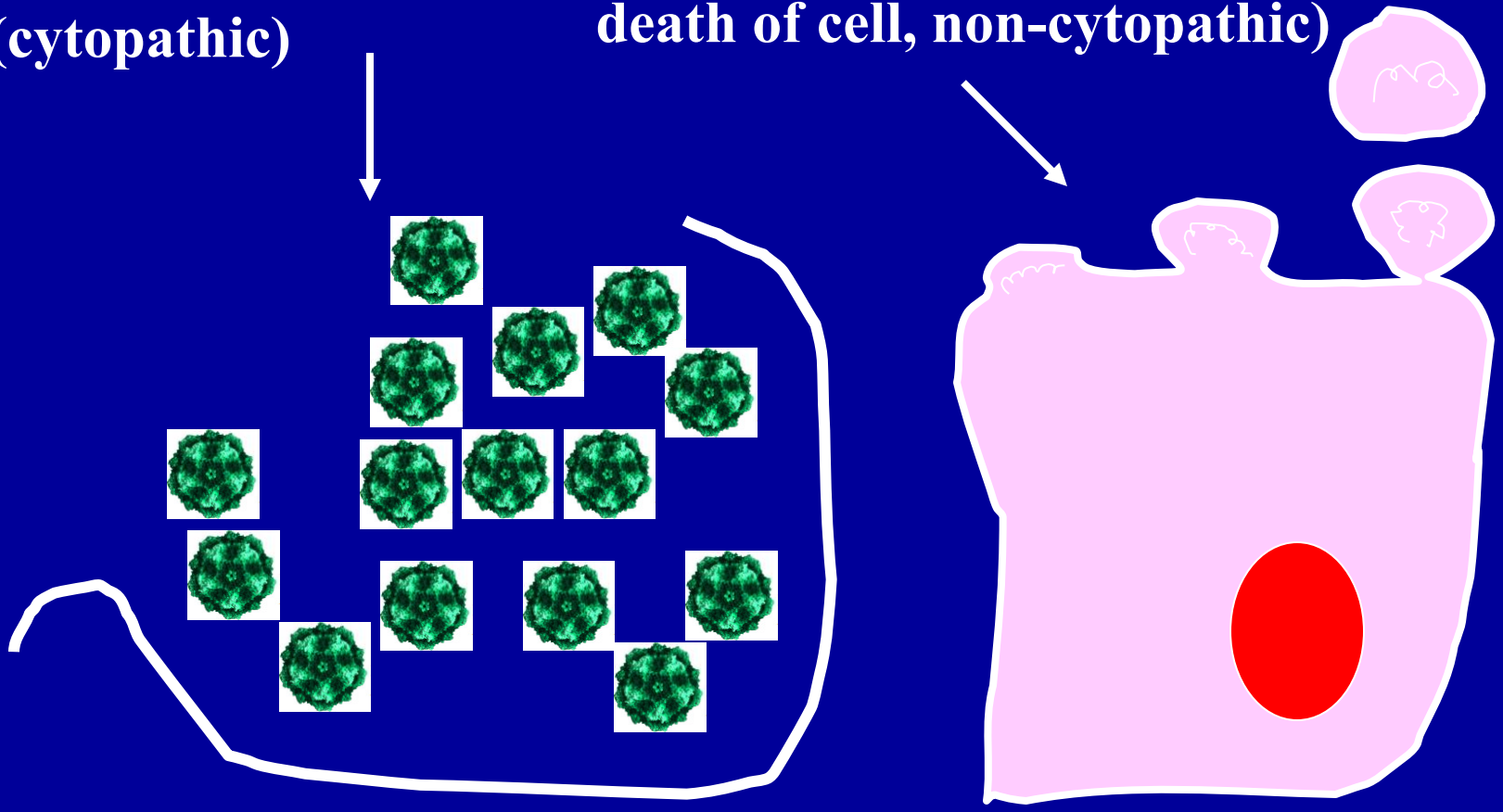


Molecular sub-typing is a bit like the parable of the blind men and the elephant – you can get an entirely different picture of what you're dealing with depending on which part of the beast you're examining!

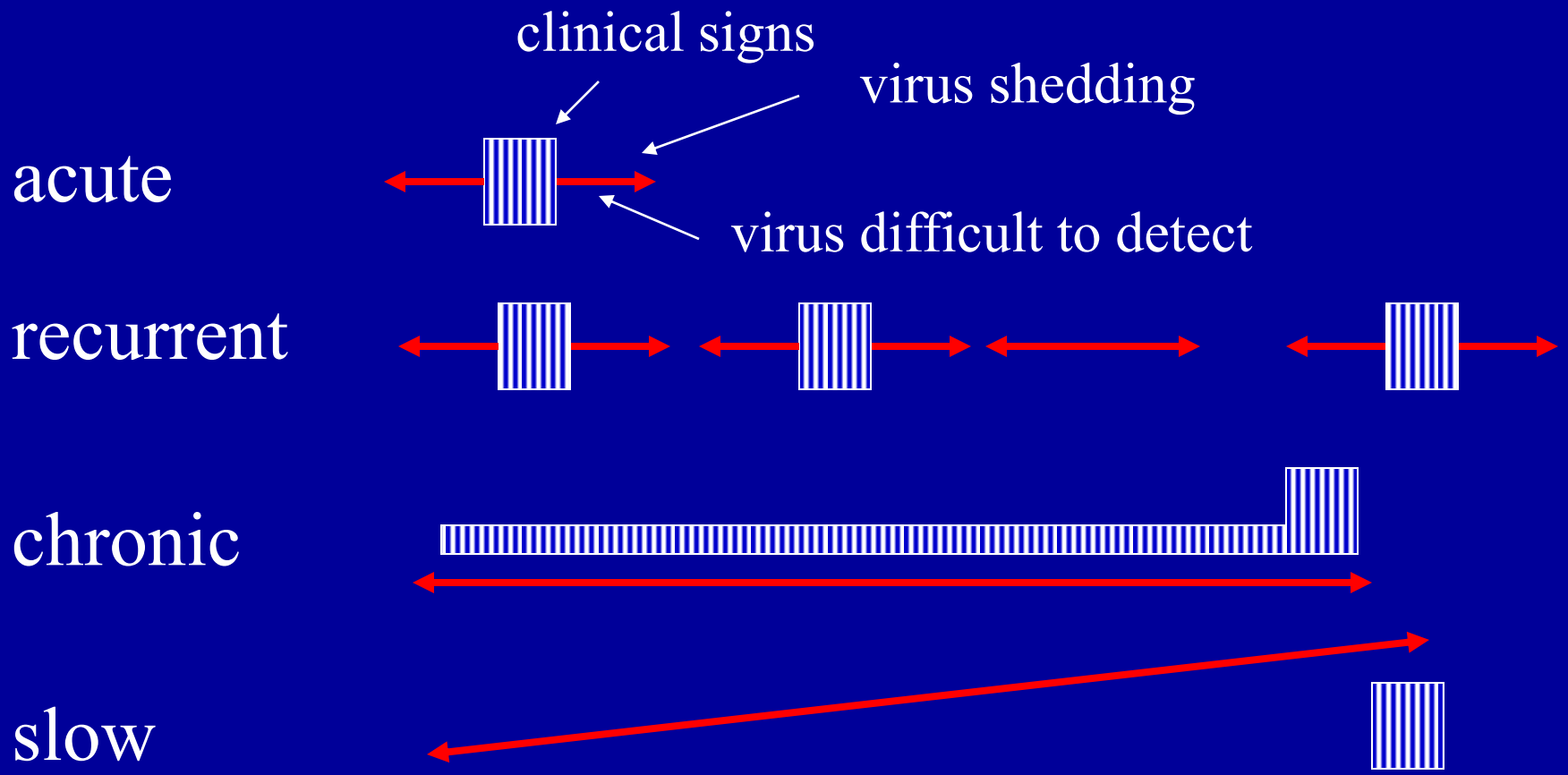
Release of virus

Release by lysis of cell (cytopathic)

or by budding (without death of cell, non-cytopathic)



Patterns of disease



Virus Infections: Some Important Viruses Cause Localized Infections and Others Systemic Infections

Enteric Viruses:

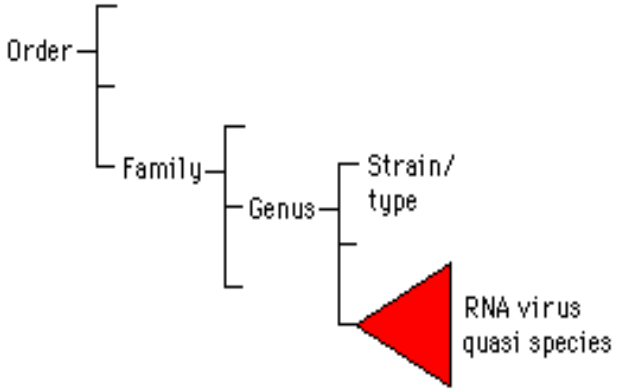
- **Localized:**
  - caliciviruses
  - astroviruses
  - adenoviruses
  - rotaviruses
- **Generalized:**
  - enteroviruses
  - hepatitis A and E viruses

Respiratory Viruses:

- **Localized:**
  - rhinoviruses
  - coronaviruses
  - Orthomyxoviruses(Flu)
  - paramyxoviruses
- **Generalized:**
  - herpesviruses
  - measles
  - mumps

How are viruses classified ?

Hierarchical virus classification: (order) family - subfamily - genus - species - strain/type



All families have the suffix viridae, e.g.:

* **Poxviridae**
* **Herpesviridae**
* **Parvoviridae**
* **Retroviridae**

Genera have the suffix virus. Within the Picornaviridae there are 5 genera:

* **enterovirus (alimentary tract), species e.g. poliovirus 1, 2, 3**
* **cardiovirus (neurotropic), species e.g. mengovirus**
* **rhinovirus (nasopharyngeal region), species e.g. Rhinovirus 1a**
* **apthovirus (cloven footed animals), species e.g. FMDV-C**
* **hepatovirus (liver), species e.g. Hepatitis A virus**

Virus naming and classification

Usually based on data available at the time of discovery:

i ***Disease they are associated with, e.g.:***
Poxvirus, Hepatitis virus, HIV, measles virus

ii ***Cytopathology they cause, e.g.:***
Respiratory Syncytial virus, Cytomegalovirus

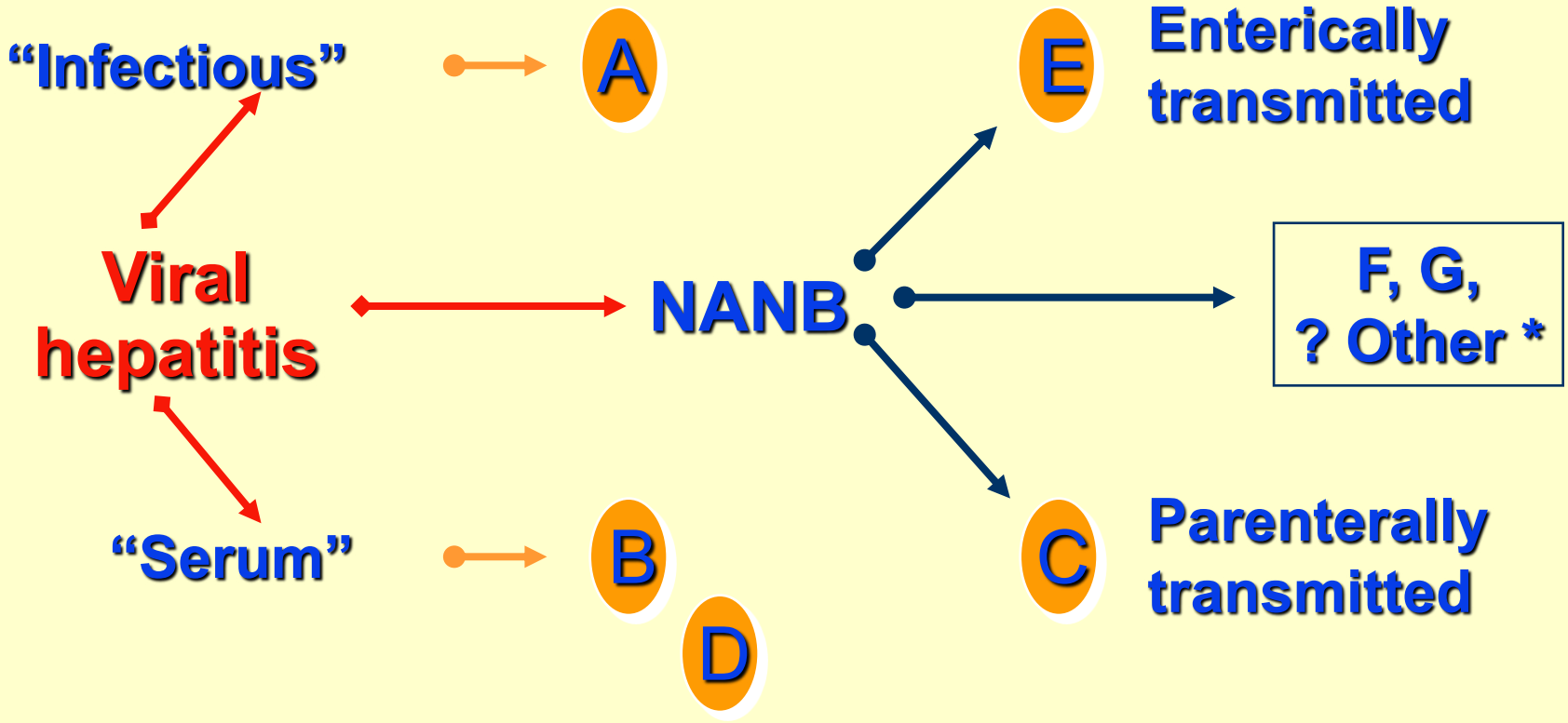
iii ***Site of isolation, e.g.:***
Adenovirus, Enterovirus, Rhinovirus

iv ***Places discovered or people that discovered them, e.g.:***
Epstein-Barr virus, Rift Valley Fever

v ***Biochemical features, e.g.:***
Retrovirus, Picornavirus, Hepadnavirus

These naming conventions can lead to confusion later, e.g.,

viral hepatitis is caused by at least 6 different viruses



*** 10-20% of cases of presumed viral hepatitis are still not accounted for**

Thus,

Different viruses can cause (nearly) the same symptoms. e.g., the *hepatitis viruses*

However, different members of the same group can cause different symptoms. e.g., the *herpes viruses*

Virus Classification is now based principally on analysis of the particle:

Morphology:

by electron microscopy

Serology:

antigenic cross-reactivity

Genetic material:

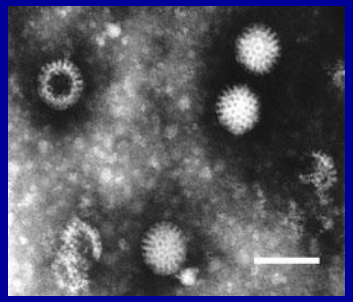
form of nucleic acid

- ssDNA (+ or - strand)
- dsDNA
- ssRNA (+ or - strand)
- dsRNA
- segmented RNA

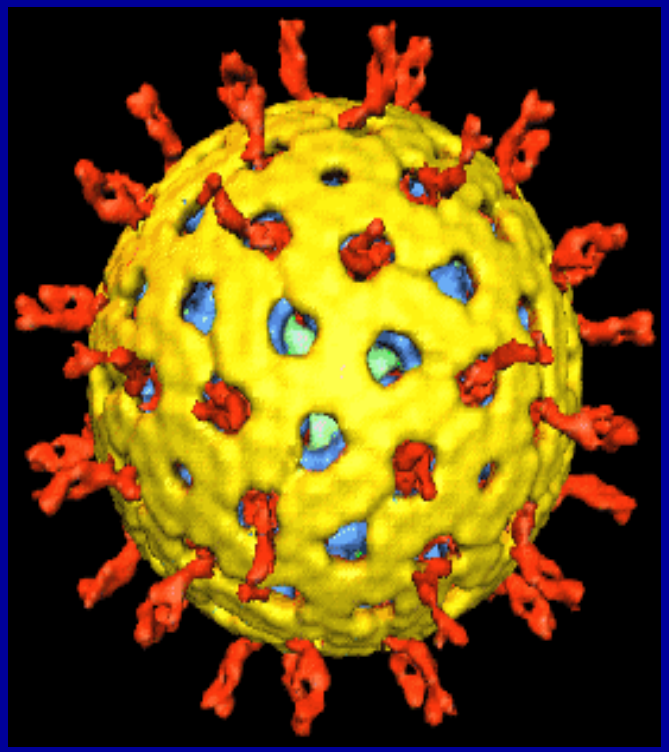
genetic organization

sequence homology

- DNA sequence
- Hybridization



Rotavirus



Viral Gastroenteritis

- It is thought that viruses are responsible for up to 3/4 of all infective diarrhoeas.
- Viral gastroenteritis is the second most common viral illness after upper respiratory tract infection.
- In developing countries, viral gastroenteritis is a major killer of infants who are undernourished. Rotaviruses are responsible for half a million deaths a year.
- Many different types of viruses are found in the gut but only some are associated with gastroenteritis

Viruses found in the gut (1)

A. Associated with gastroenteritis

- Rotaviruses
- Adenoviruses 40 41
- Caliciviruses
- Norwalk like viruses or SRSV (Small Round Structured Viruses)
- Astroviruses
- SRV (Small Round Viruses)
- Coronaviruses
- Toroviruses

Viruses found in the gut (2)

B. Found in the gut, not normally associated with gastroenteritis

- Polio
- Coxsackie A
- Coxsackie B
- Echo
- Enteroviruses 68-71
- Hepatitis A
- Hepatitis E
- Adenoviruses 1-39
- Reoviruses

C. Found in the gut as opportunistic infection

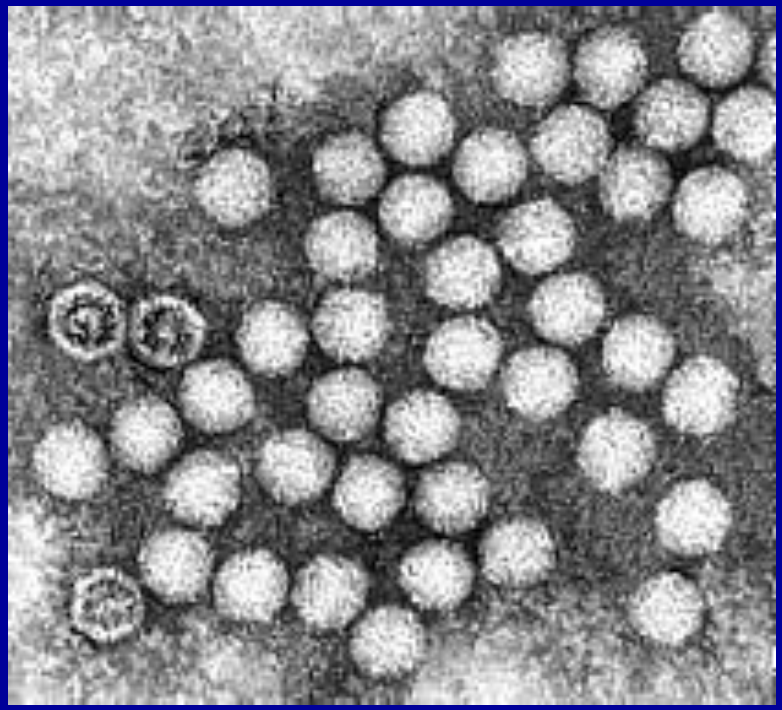
- CMV
- HSV
- VZV
- HIV

Viruses Associated with Respiratory Infections

Syndrome	Commonly Associated Viruses	Less Commonly Associated Viruses
Colds	Rhinoviruses, Coronaviruses	Influenza and parainfluenza viruses, enteroviruses, adenoviruses
Influenza	Influenza viruses	Parainfluenza viruses, adenoviruses
Croup	Parainfluenza viruses	Influenza virus, RSV, adenoviruses
Bronchiolitis	RSV	Influenza and parainfluenza viruses, adenoviruses
Bronchopneumonia	Influenza virus, RSV, Adenoviruses	Parainfluenza viruses, measles, VZV, CMV

Enteroviruses

- Icosahedral shape
- ~27-30 nm diameter
- single-stranded +sense RNA
  - about 7,500 nucleotides
- icosahedral protein coat (capsid)
  - 4 capsid proteins: VP1, VP2, VP3, VP4 (all cleaved from VP0)
- >71 antigenically distinct human types
  - polioviruses (3 types)
  - coxsackie B viruses (6 types)
  - coxsackie A viruses (23 types)
  - echoviruses (31 types)
- distinct animal enteroviruses
- Cause enteric illness
- Some cause respiratory illness



Enteroviruses

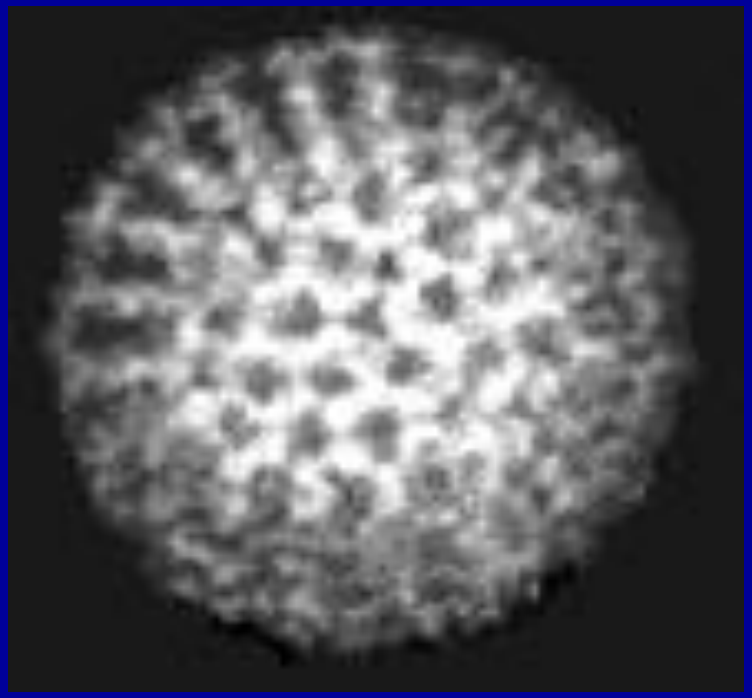
- Enteroviruses are a genus of the picornavirus family which replicate mainly in the gut.
- Single stranded naked RNA virus with icosahedral symmetry
- Unlike rhinoviruses, they are stable in acid pH
- capsid has 60 copies each of 4 proteins, VP1, VP2, VP3 and VP4 arranged with icosahedral symmetry around a positive sense genome. At least 71 serotypes are known: divided into 5 groups
  - Polioviruses
  - Coxsackie A viruses
  - Coxsackie B viruses
  - Echoviruses
  - Enteroviruses (more recently, new enteroviruses subtype have been allocated sequential numbers (68-71))

Diseases associated with Enteroviruses

Syndrome	Polio	Cox A	Cox B	Echo
Paralytic disease	+	+	+	+
Meningitis-encephalitis	+	+	+	+
Carditis	+	+	+	+
Neonatal disease	-	-	+	+
Pleurodynia	-	-	+	-
Herpangina	-	+	-	-
Rash disease	-	+	+	+
Haemorr. conjunctivitis	-	+	-	-
Respiratory infections	+	+	+	+
Undifferentiated fever	+	+	+	+
Diabetes/pancreatitis	-	-	+	-

Reovirus and Rotaviruses

- ~spherical; icosahedral
- ~75-80 nm diameter
- double-layered capsid
- nucleic acid:
  - double-stranded RNA
  - 11 segments rota)
  - 10 segments (reo)
  - electropherotypes
- 7 Groups
  - Subgroups, serotypes
- Cause enteric illness
  - Group A most important in humans (children)
  - Group C causes sporadic illness
  - Group B has caused large outbreaks (adults), rare

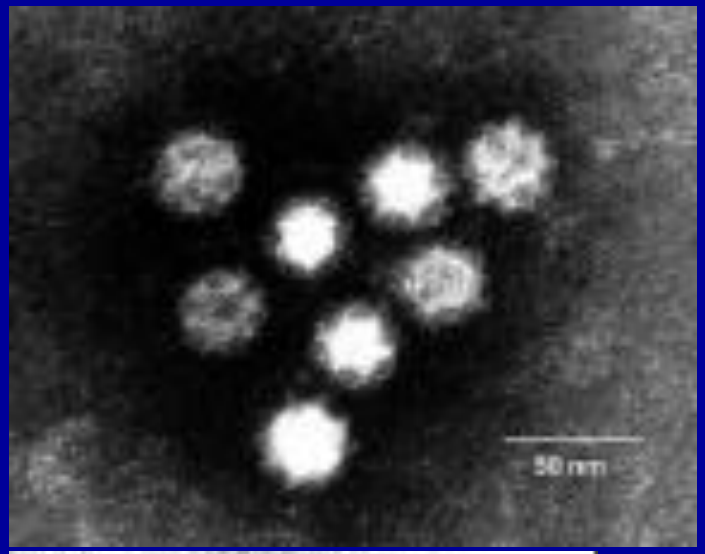


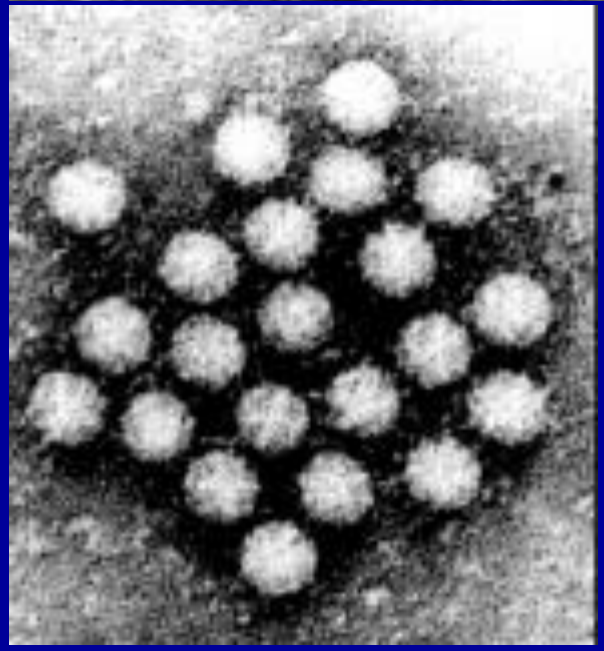
Rotaviruses

- Naked double stranded RNA viruses, 80 nm in diameter
- also found in other mammals and birds, causing diarrhoea
- account for 50-80% of all cases of viral gastroenteritis
- usually endemic, but responsible for occasional outbreaks
- causes disease in all age groups but most severe symptoms in neonates and young children. Asymptomatic infections common in adults and older children. Symptomatic infections again common in people over 60
- up to 30% mortality rate in malnourished children, responsible for up to half a million deaths per year

Caliciviruses: Noroviruses and Sappoviruses

- Icosahedral
- "structured"; cup-like surface morphology
- 30-35 nm diameter
- ss(+) RNA, ~7.7 KB
- 1 major capsid polypeptide, ~60 kD
- minor protein, ~30 kD
- 3 major HuCV groups
  - G 1 and 2; "Sapporo-like"
  - Genetically diverse/variable
- No culture (except in humans)
- Distinct animal caliciviruses
  - some genetically similar to human caliciviruses
  - cross-species transmission?



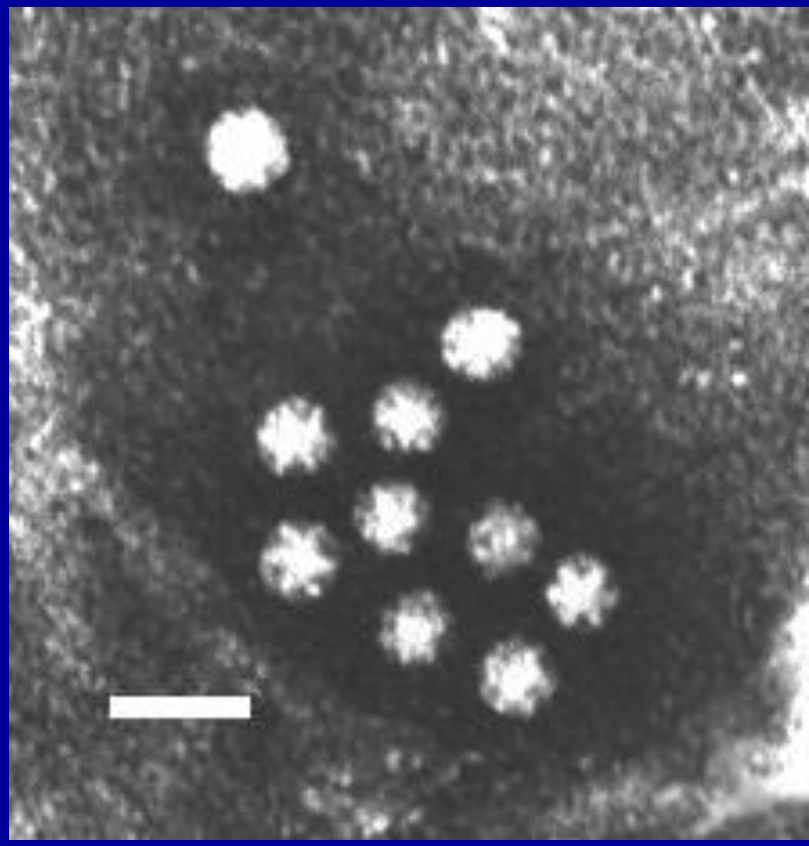


Just How Much Diarrhea is That?

- In the US:
  - 12.7 million cases
- International:
  - 200 million cases
- 12.7 million cases x 4 episodes/day x 3 days duration x 200ml/episode = 3.6×10^{11} ml of diarrhea or 105 million gallons or 6 minutes of flow over Niagra Falls

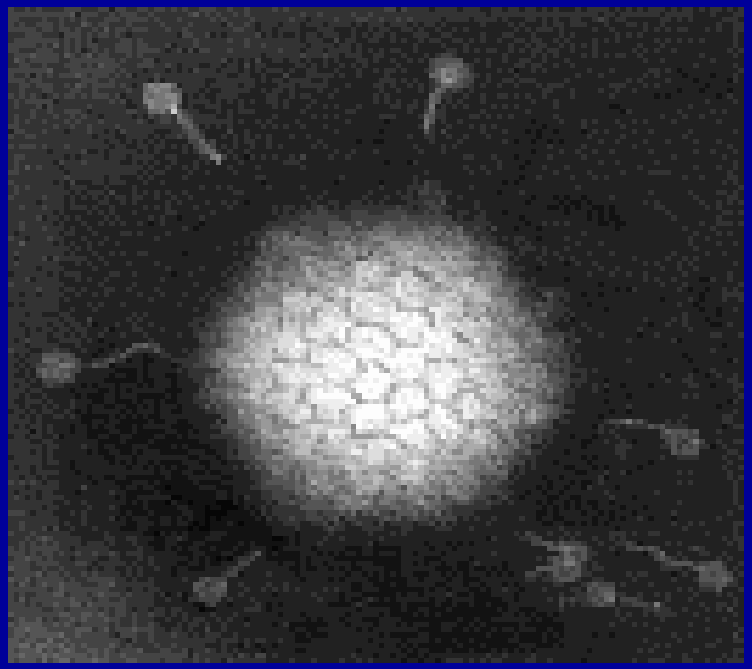
Astroviruses

- Small RNA viruses, named because of star-shaped surface morphology, 28 nm in diameter
- associated with cases of endemic gastroenteritis, usually in young children and neonates. Can cause occasional outbreaks.
- responsible for up to 10% of cases of gastroenteritis
- similar disease to rota and adenoviruses
- most people have antibodies by the age of three.
- diagnosed by electron microscopy only, often very difficult because of small size



ADENOVIRUSES:

- icosahedral
- ~80 nm diameter
- double-stranded, linear DNA
- protein coat contains at least 10 proteins
  - Hexons, pentons, minor polypeptides
  - attachment fibers with knobs
- At least 41 human adenoviruses
  - types 1-39 mostly respiratory
    - but fecally shed
  - types 40 and 41 are enteric
- Often the most prevalent viruses in treated sewage
  - resistance to treatment?
- Distinct animal adenoviruses



Enteric Adenoviruses

- associated with cases of endemic gastroenteritis, usually in young children and neonates. Can cause occasional outbreaks.
- possibly the second most common viral cause of gastroenteritis (7-15% of all endemic cases)
- similar disease to rotaviruses
- most people have antibodies against enteric adenoviruses by the age of three
- diagnosed by electron microscopy or by the detection of adenovirus antigens in faeces by ELISA or other assays.

Other Clinical Syndromes

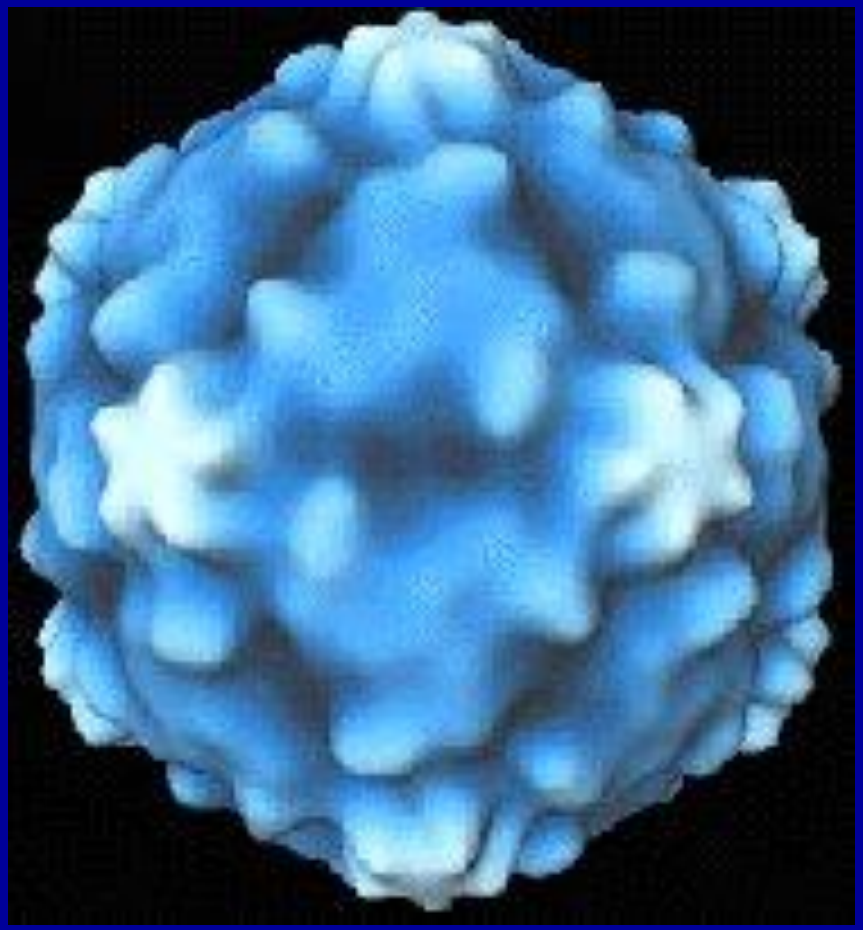
1. Pharyngitis 1, 2, 3, 5, 7
2. Pharyngoconjunctival fever 3, 7
3. Acute respiratory disease of recruits 4, 7, 14, 21
4. Pneumonia 1, 2, 3, 7
5. Follicular conjunctivitis 3, 4, 11
6. Epidemic keratoconjunctivitis 8, 19, 37
7. Petussis-like syndrome 5
8. Acute haemorrhaghic cystitis 11, 21
9. Acute infantile gastroenteritis 40, 41
10. Intussusception 1, 2, 5
11. severe disease in AIDS and other immunocompromized patients 5, 34, 35
12. Meningitis 3, 7

Common Cold Viruses

- Common colds account for one-third to one-half of all acute respiratory infections in humans
- Rhinoviruses are responsible for 30-50% of common colds, coronaviruses 10-30%
- The rest are due to adenoviruses, enteroviruses, RSV, influenza, and parainfluenza viruses, which may cause symptoms indistinguishable to those of rhinoviruses and coronaviruses

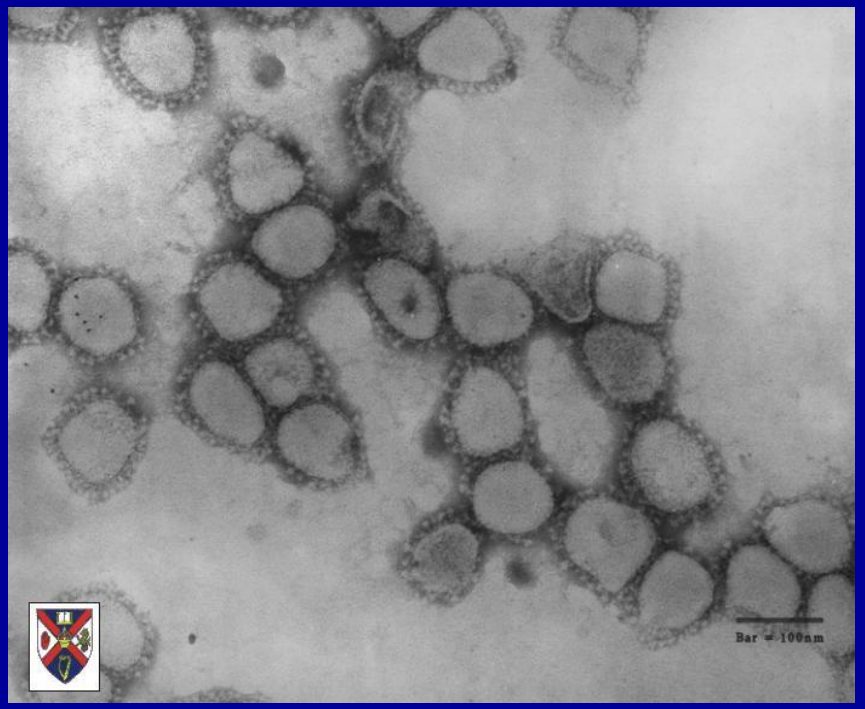
Rhinoviruses

- Spherical
  - 27-30 nm diamter
- +ssRNA genome
  - ~7.2kb
- Nonenveloped, icosahedral capsid
- 50% of Common Colds
- 105 serotypes

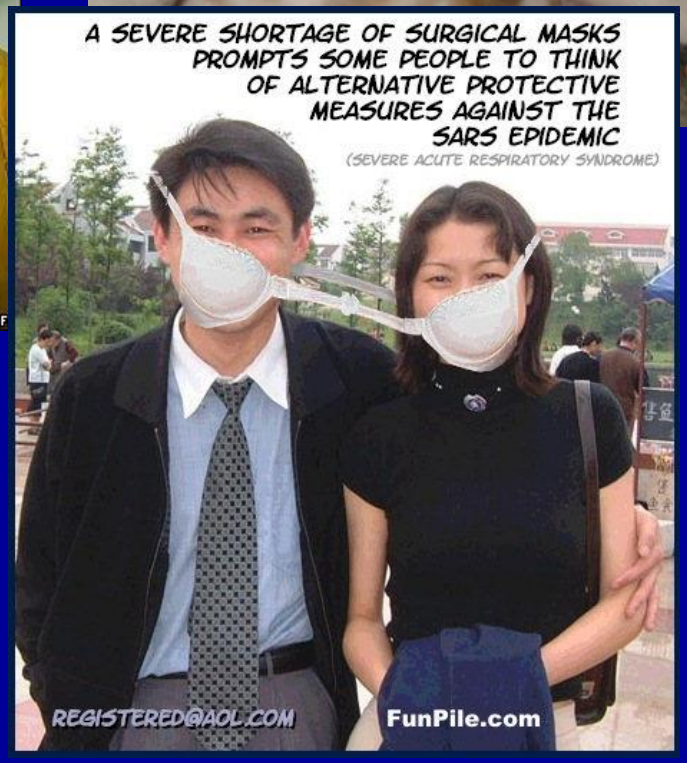


Coronaviruses

- Irregularly shaped
  - 60-220 nm diameter
- +ssRNA genome (27-31 kb)
- Enveloped particles with loosely wound nucleocapsid
  - characteristic “club-shaped” peplomers
- 10 % of Common colds

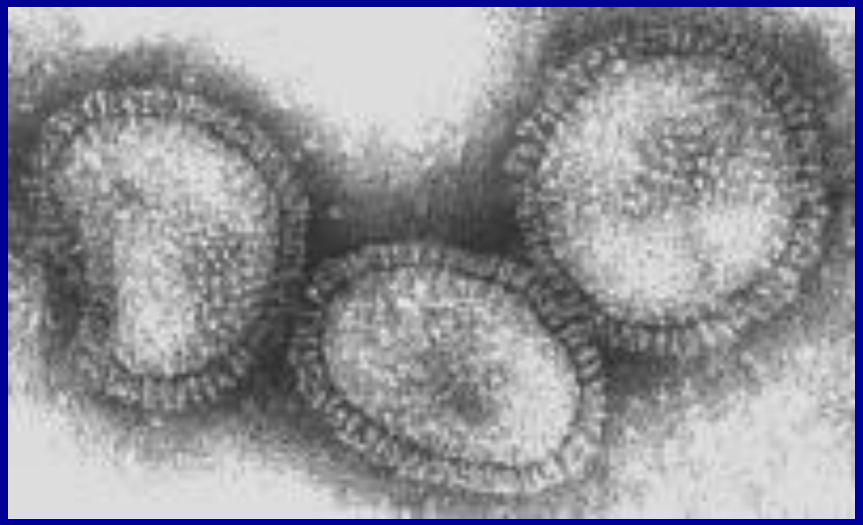


Severe Acute Respiratory Syndrome (SARS)



Influenza Viruses

- Pleomorphic, spherical filamentous forms occur
  - 50-120 nm diameter, or 20 nm diameter and 200-300 nm long
- Segmented, linear -ssRNA genome
  - 7 to 8 segments
- Enveloped, filamentous nucleocapsids
  - Envelope is lipid bilayer with ~500 spikes for attachment
    - Hemagglutinin
    - Neuraminidase
- Causes “the flu”



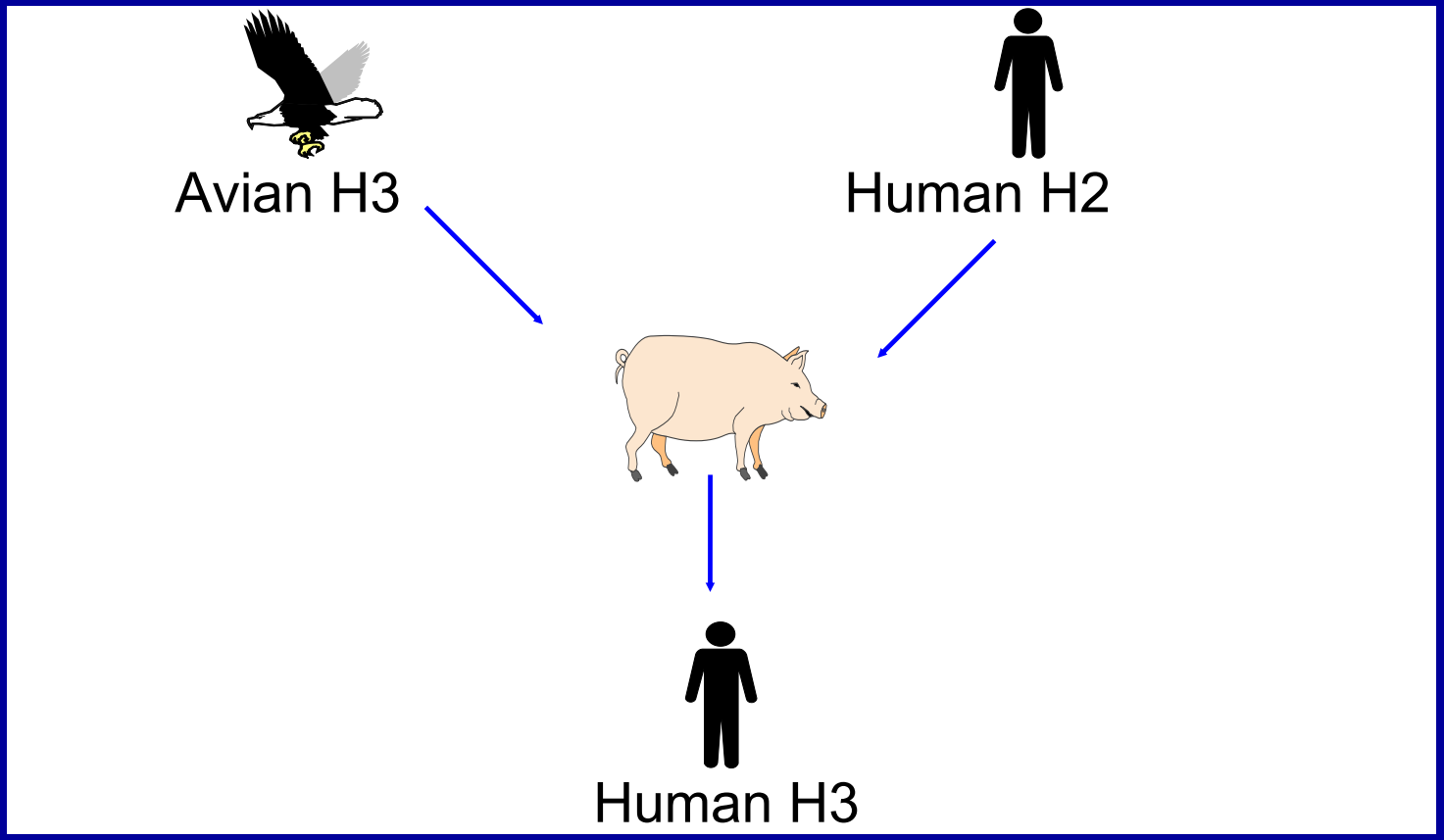
Influenza A Virus

- Undergoes antigenic shifts and antigenic drifts with the haemagglutinin and neuraminidase proteins.
- Antigenic shifts of the haemagglutinin results in pandemics. Antigenic drifts in the H and N proteins result in epidemics.
- Usually causes a mild febrile illness
- Death may result from complications such as viral/bacterial pneumonia

Theories Behind Antigenic Shift

1. Reassortment of the H and N genes between human and avian influenza viruses through a third host
2. Recycling of pre-existing strains
3. Gradual adaptation of avian influenza viruses to human transmission

Reassortment



Arthropod-borne Viruses

Arthropod-borne viruses (arboviruses) are viruses that can be transmitted to man by arthropod vectors. The WHO definition is as follows

"Viruses maintained in nature principally, or to an important extent, through biological transmission between susceptible vertebrate hosts by haematophagus arthropods or through transovarian and possibly venereal transmission in arthropods."

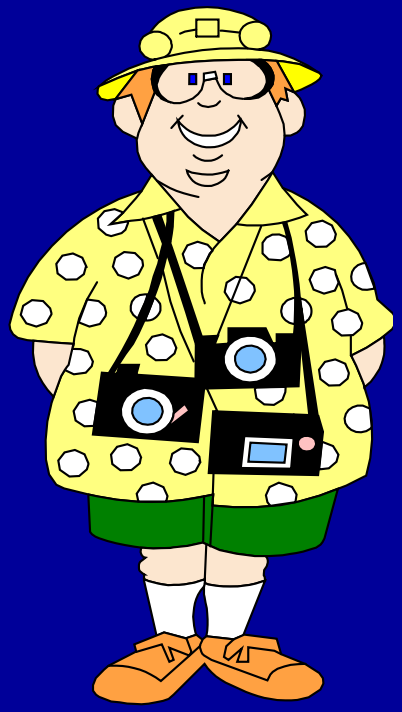
Arboviruses belong to three families

1. Togaviruses e.g. EEE, WEE, and VEE

2. Bunyaviruses e.g. Sandfly Fever, Rift Valley Fever, Crimean-Congo Haemorrhagic Fever

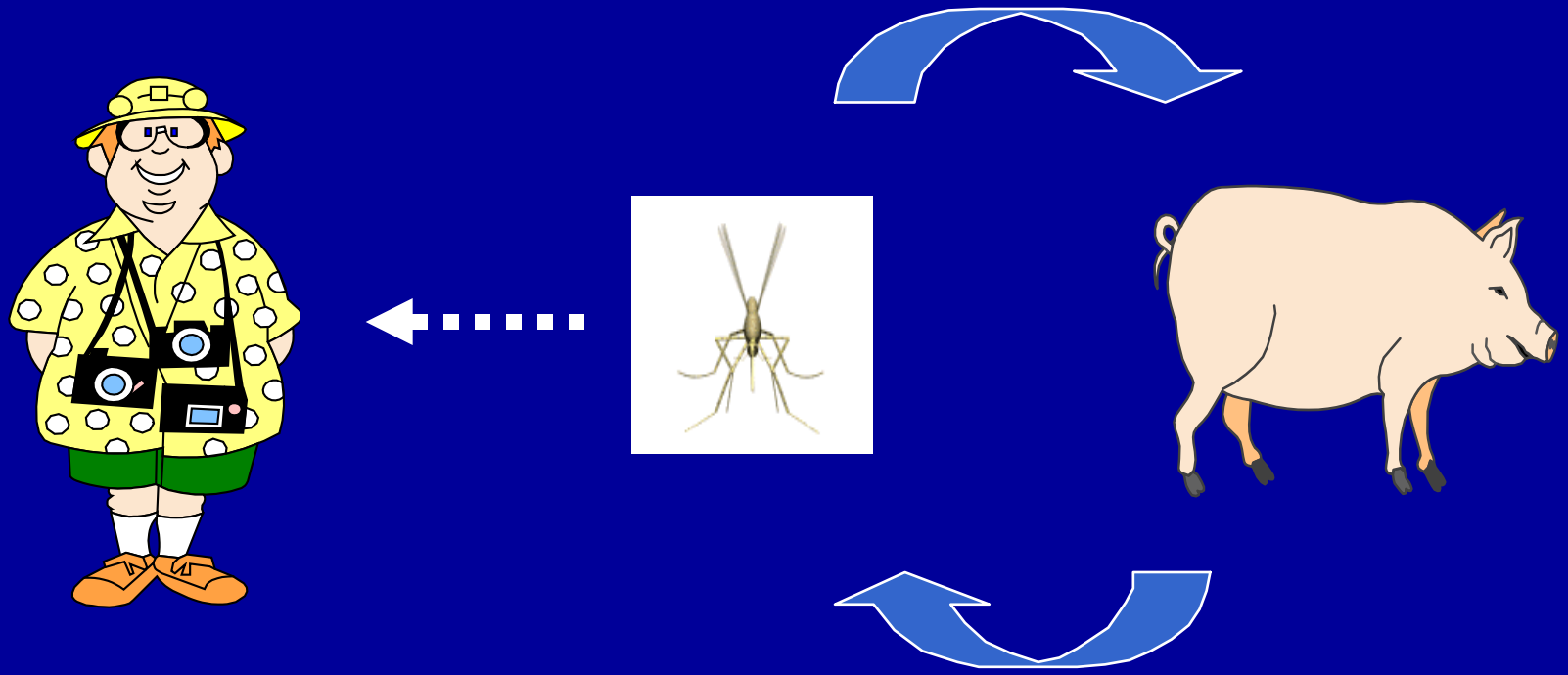
3. Flaviviruses e.g. Yellow Fever, dengue, Japanese Encephalitis

Man-Arthropod-Man Cycle



e.g. dengue, urban yellow fever. Reservoir may be in either man or arthropod vector. In the latter transovarial transmission may take place.

Animal-Arthropod-Man Cycle



e.g. Japanese encephalitis, EEE, WEE, jungle yellow fever. The reservoir is in an animal. The virus is maintained in nature in a transmission cycle involving the arthropod vector and animal. Man becomes infected incidentally.

Arthopod Vectors

Mosquitoes

Japanese encephalitis, dengue, yellow fever, St. Louis encephalitis, EEE, WEE, VEE etc.

Ticks

Crimean-Congo haemorrhagic fever, various tick-borne encephalides etc.

Sandflies

Sicilian sandfly fever, Rift valley fever

Animal Reservoirs

In many cases, the actual reservoir is not known. The following animals are implicated as reservoirs

Birds	Japanese encephalitis, St Louis encephalitis, EEE, WEE
Pigs	Japanese encephalitis
Monkeys	yellow fever
Rodents	VEE, Russian Spring-Summer encephalitis

Diseases Caused

Fever and rash - this is usually a non-specific illness resembling a number of other viral illnesses such as influenza, rubella, and enterovirus infections. The patients may go on to develop encephalitis or haemorrhagic fever

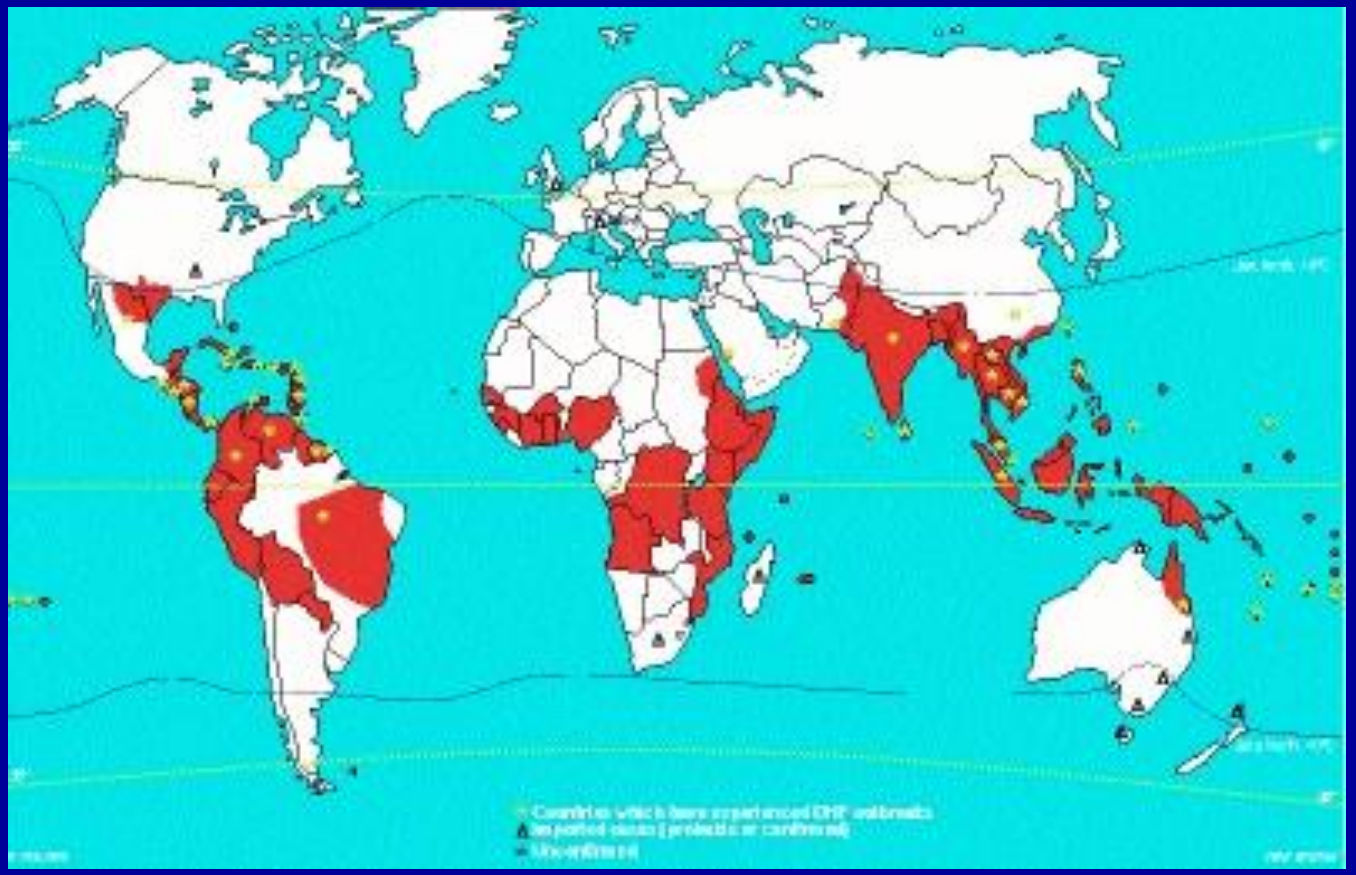
Encephalitis - e.g. EEE, WEE, St Louis encephalitis, Japanese encephalitis

Haemorrhagic fever - e.g. yellow fever, dengue, Crimean-Congo haemorrhagic fever

Dengue

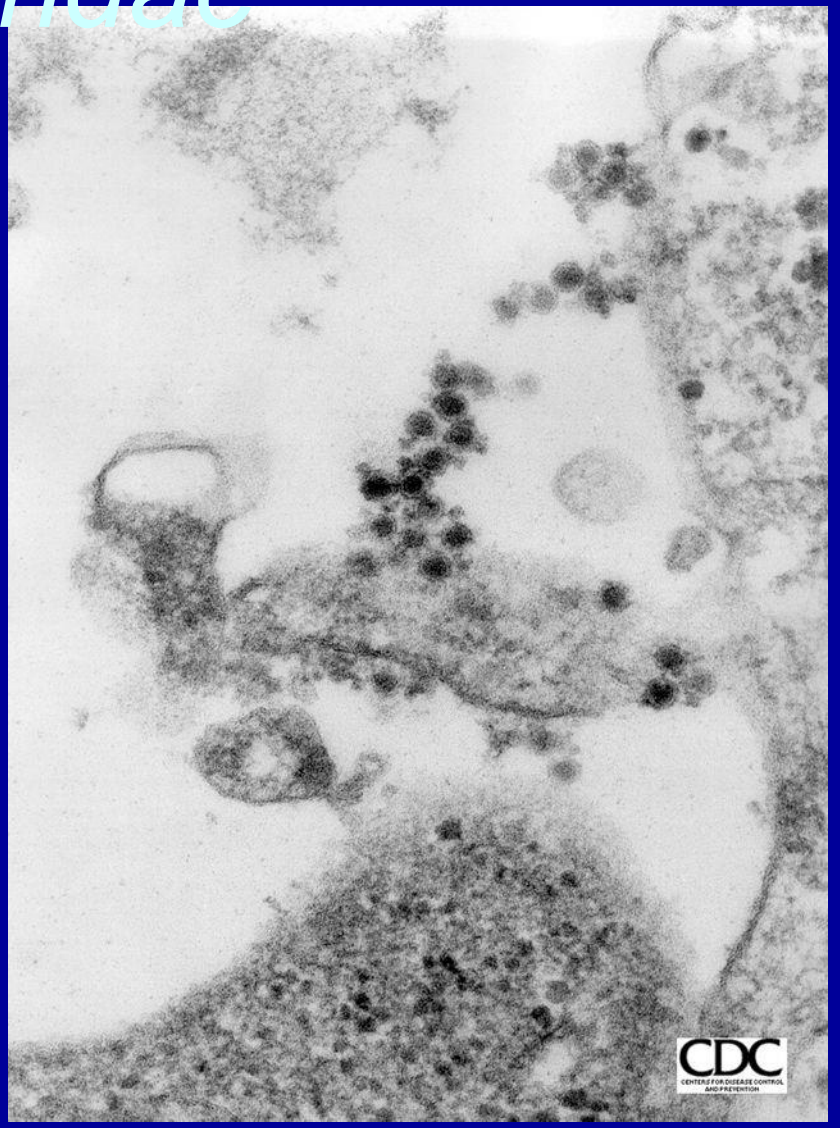
- Dengue is the biggest arbovirus problem in the world today with over 2 million cases per year. Dengue is found in SE Asia, Africa and the Caribbean and S America.
- Flavivirus, 4 serotypes, transmitted by Aedes mosquitoes which reside in waterfilled containers.
- Human infections arise from a human-mosquitoe-human cycle
- Classically, dengue presents with a high fever, lymphadenopathy, myalgia, bone and joint pains, headache, and a maculopapular rash.
- Severe cases may present with haemorrhagic fever and shock with a mortality of 5-10%. (Dengue haemorrhagic fever or Dengue shock syndrome.)

Distribution of Dengue



Flaviviridae

- 40-60 nm
- enveloped
- +ve sense ssRNA
- polyprotein, processed by proteolysis

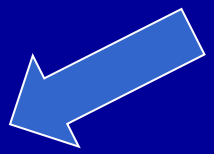


http://www.cdc.gov/ncidod/dvbid/westnile/virus.htm

BVD, Hog cholera, Border disease

Pestiviruses

Flaviviridae



Flaviviruses

Japanese encephalitis
St. Louis encephalitis
Dengue
West Nile virus
(arthropods, biological vectors)

Hepatitis C virus

Zoonotic Viruses

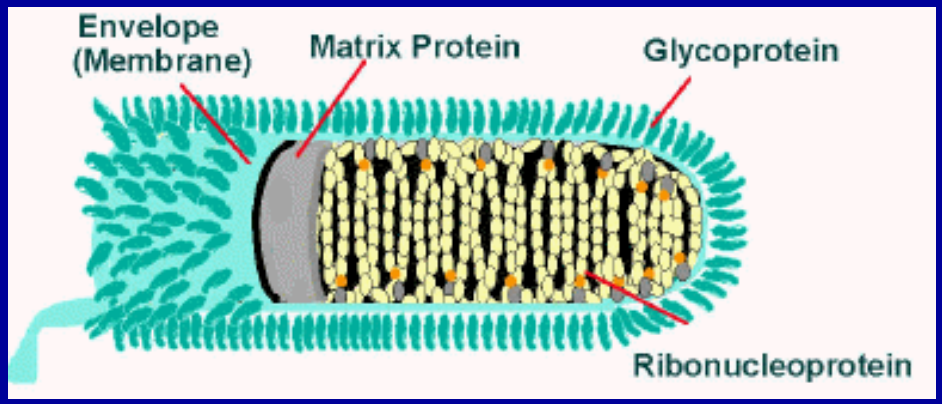
- Zoonoses are diseases of vertebrate animals that can be transmitted to man: either directly or indirectly through an insect vector.
- When an insect vector is involved, the disease is also known as an arboviral disease.
- However, not all arboviral diseases are zoonosis: where the transmission cycle takes place exclusively between insect vector and human e.g. dengue and urban yellow fever.
- Examples of viral zoonoses that can be transmitted to man directly include rabies, hantaviruses, lassa and ebola fevers.

Rabies Virus

- member of the Lyassavirus of the Rhabdoviridae
- ssRNA enveloped virus, characteristic bullet-shaped appearance with 6-7 nm spike projections.
- virion 130-240nm * 80nm
- -ve stranded RNA codes for 5 proteins; G, M, N, L, S
- Exceedingly wide range of hosts
- There are 5 other members of Lyassavirus : Mokola, Lagosbat, Duvenhage, EBL-1, and EBL-2
- Duvenhage and EBL-2 have been associated with human rabies.

Rabies Virus

Rabies virus particles



Structure of rabies virus (Source: CDC)

Epidemiology

- Rabies is a zoonosis which is prevalent in wildlife. The main animals involved differs from continent to continent.

Europe	fox, bats
Middle East	wolf, dog
Asia	dog
Africa	dog, mongoose, antelope
N America	foxes, skunks, raccoons, insectivorous bats
S America	dog, vampire bats

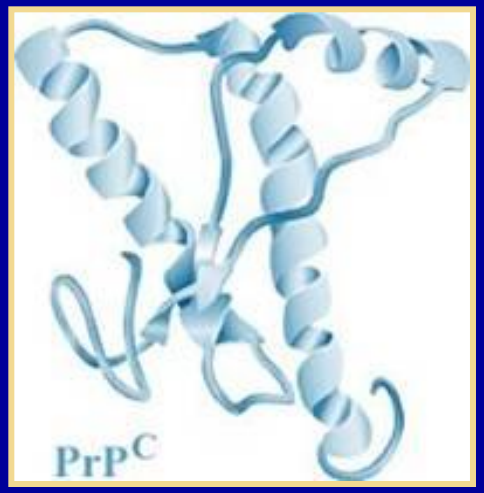
Spongiform Encephalopathies and Prions

Prion

- Smaller than smallest known virus
- Not yet completely characterized
- Most widely accepted theory
  - Prion = Proteinaceous infectious particle
- Normal Protein
  - PrP^{C} (C for cellular)
  - Glycoprotein normally found at cell surface inserted in plasma membrane

Normal protein

- Secondary structure dominated by alpha helices
- Easily soluble
- Easily digested by proteases
- Encoded by PRNP gene (in humans)
  - Located on human chromosome 20

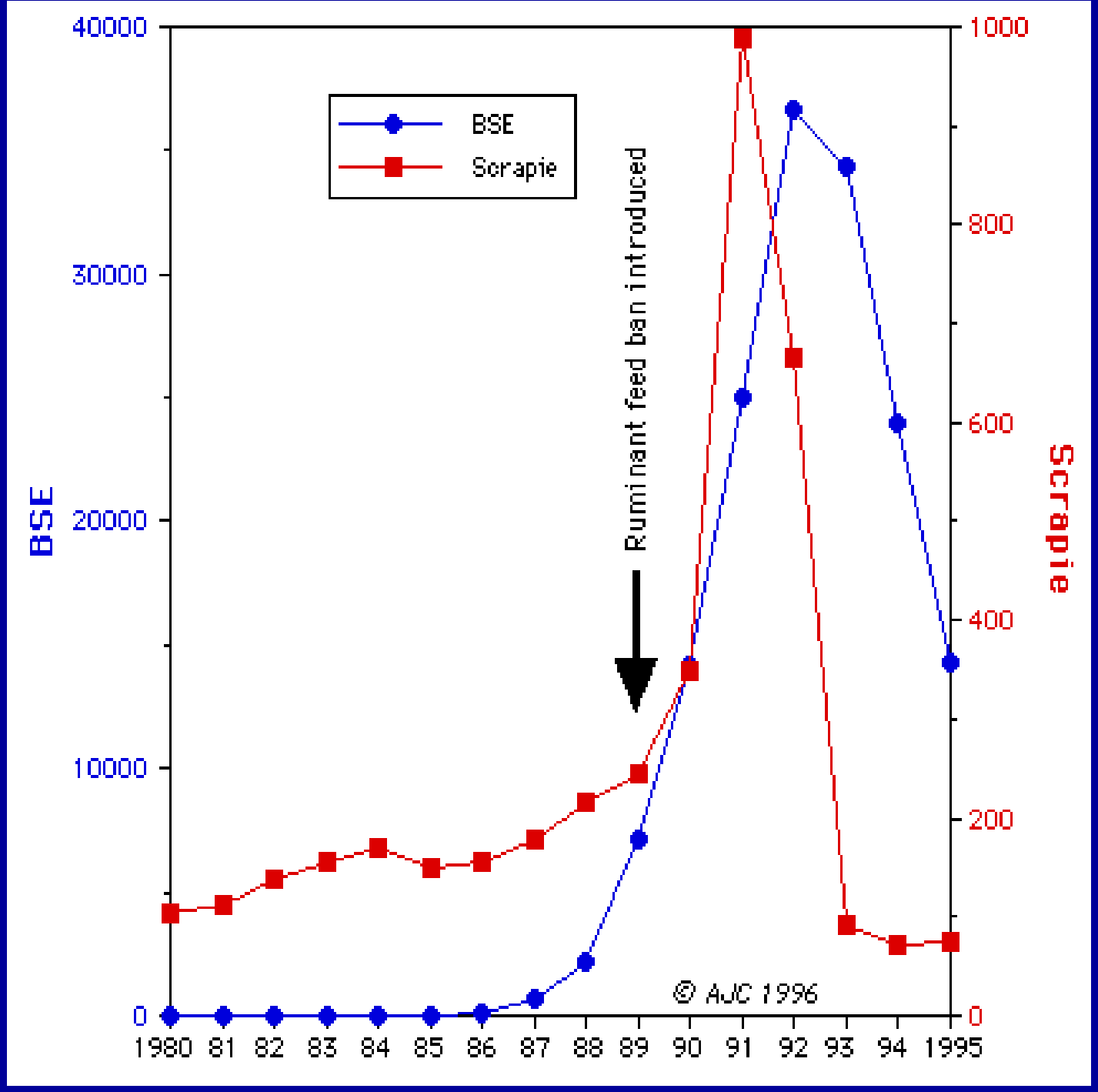


Abnormal Protein

- Insoluble in all but strongest solvents
- Highly resistant to digestion by proteases
  - Survives in tissues post-mortem
- Extremely resistant
  - Heat, normal sterilization processes, sunlight
- No detectable immune response

spongiform encephalopathies of humans and other animals

- humans
  - Kuru (Fore people in New Guinea)
  - Creutzfeldt-Jakob disease (CJD)
  - Gerstmann-Straussler-Scheinker (GSS)
  - fatal familial insomnia
  - new variant CJD
- Animals
  - Scrapie
  - exotic ungulate encephalopathy
  - bovine spongiform encephalopathy (BSE)
  - transmissible mink encephalopathy
  - feline spongiform encephalopathy
  - chronic wasting disease (CWD)


BSE
Scrapie
Ruminant feed ban introduced
© AJC 1996
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Scrapie
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