



Medical Virology for 2nd Year M.D. Students



Respiratory, GI and CNS Viruses

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Paramyxoviridae



- ❖ The paramyxoviruses include the most important agents of **respiratory infections** of **infants and young children**, as well as the causative agents of two of the common contagious diseases of childhood (**mumps** and **measles**).
- ❖ All members of the *Paramyxoviridae* family **initiate** infection **via the respiratory tract**.
- ❖ The paramyxoviruses are enveloped **-ss RNA viruses** with non-segmented genome.



Acute respiratory infections and pneumonia are responsible for the deaths of 4 million children younger than 5 years of age worldwide.



Togaviridae



❖ The togaviruses are **enveloped** +ss RNA viruses that contribute significantly to human disease.

❖ *Togaviridae* is divided into two genera:
Alphavirus and **Rubivirus**.





Alphavirus



- The alphaviruses are **arthropod-borne** viruses (**arboviruses**), which are transmitted to humans and domestic animals by **mosquitoes**.
- *The majority of infections are subclinical*, however, several clinical syndromes are associated with alphavirus infections of humans. These include: **acute encephalitis** (equine encephalitis viruses); **acute arthropathy** (**Chikungunya virus**) and a febrile illness with a **flulike syndrome**.





Rubella virus



- Rubella (German measles; 3-day measles) is an acute febrile illness characterized by a rash and lymphadenopathy that affects children and young adults.
- **In 20–50% of cases, the primary infection is subclinical.** It is the mildest of common viral exanthems. However, infection during early pregnancy may result in **serious abnormalities** of the fetus including congenital malformations and mental retardation.
- The consequences of rubella in utero are referred to as the **congenital rubella syndrome.**



Rubella (German Measles)



- Rubella usually begins with malaise, low-grade fever, and a **morbiliform (red macules) rash** appearing on the same day. The rash starts on the face, extends over the trunk and extremities, **and rarely lasts more than 3 days**. No feature of the rash is pathognomonic for rubella.



- Unless an epidemic occurs, the disease is difficult to diagnose clinically because the rash caused by other viruses (e.g. enteroviruses) is similar.



Rubella (German Measles)

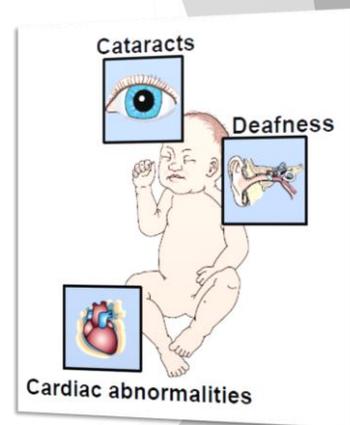
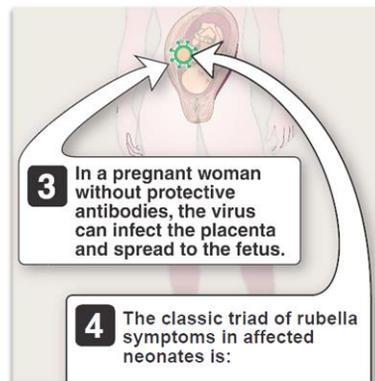
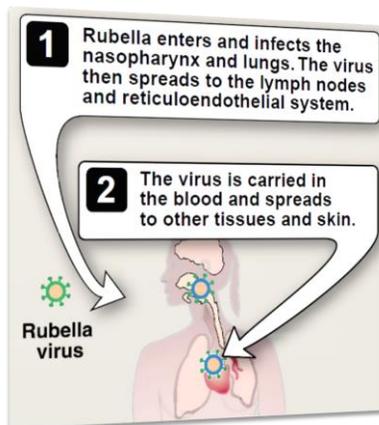


- Transient arthralgia and arthritis are commonly seen in adults, especially women.
- Rubella antibodies appear in the serum of patients as the rash fades.
- One attack of the disease confers **lifelong immunity** because only one antigenic type of the virus exists.
- [A rubella vaccine is available.](#)



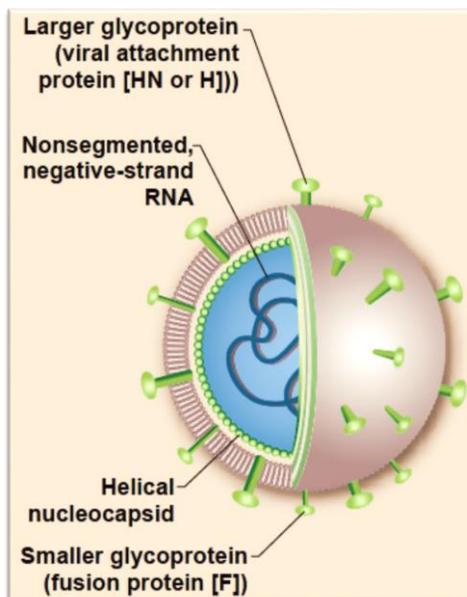


Congenital rubella syndrome





Paramyxoviridae





Classification of *Paramyxoviridae*



Subfamily	<i>Paramyxovirinae</i>				<i>Pneumovirinae</i>	
Genus	Respirovirus	Rubulavirus	Morbillivirus	Henipavirus	Pneumovirus	Metapneumovirus
Species	PIV-1, PIV-3	Mumps, PIV-2, PIV-4	Measles	Hendra, Nipah	RSV	Metapneumovirus

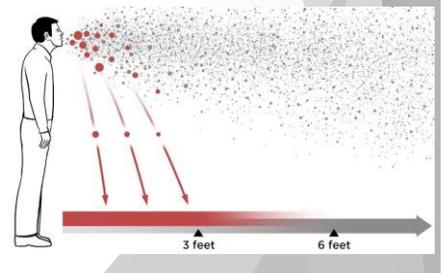




Measles virus



- The cellular receptor for measles virus is **CD46**.
- Measles virus is transmitted by sneeze- or cough-produced **respiratory droplets**.
- The virus is **extremely infectious**, and almost all infected individuals develop a clinical illness.
- Measles virus replicates initially in the respiratory epithelium and then in various lymphoid organs.





Measles (Rubeola, First Disease)



- Measles begins with a prodrome of fever, upper respiratory tract symptoms, and conjunctivitis.
- A few days later, specific signs develop; first, **Koplik spots** (small white spots on bright red mucous membranes of the mouth and throat) and then a **generalized macular rash**, beginning at the head and traveling slowly to the lower extremities.





Measles (Hard Measles, 10-day measles)



- Soon after the rash appears, the patient is no longer infectious.
- The major morbidity and mortality caused by measles are associated with various complications of infection, especially **pneumonia** and **encephalitis**.
- The most important of these is **postinfectious encephalomyelitis**, which is estimated to affect 1 of 1,000 cases of measles, usually occurring within two weeks after the onset of the rash. This is an **autoimmune disease** associated with an immune response to **myelin basic protein**.



Measles Dx and Prevention



- In most cases, diagnosis can be achieved **clinically**, especially in an epidemic situation.
- The presence of **Koplik spots** provides a definitive diagnosis.
- Measles is usually a disease of childhood, and is followed by life-long immunity (single serotype).
- A live attenuated measles vaccine is available.



Mumps virus



يسمى في الكويت والامارات خَاز بَاز، وفي مصر أبو الكفوف، ويسمى في بعض الدول العربية أبو كعاب أو أبو كعب، كما يسمى في بعض مناطق فلسطين أبو داج أو أبو دغيم ويسمى باليمن صنجار أو رؤطين، وفي السودان أبوعديلات، وفي الجزائر أبوشوفان وفي تونس القلقوم و بوغبة



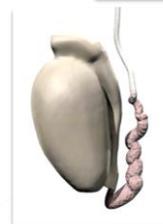
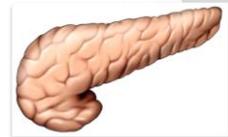
- Mumps is an acute contagious disease characterized by enlargement of one or both salivary glands.
- Mumps virus mostly causes a mild childhood disease, but in adults complications including meningitis and orchitis are fairly common.
- More than one-third of all mumps infections are **asymptomatic**.



Mumps



- The virus is spread by **respiratory droplets**.
The classic clinical presentation and diagnosis revolve around infection and swelling of the salivary glands, primarily the parotid glands.
- However, infection is widespread in the body and may involve not only the salivary glands but also the **pancreas, CNS, and testes**.
Orchitis (inflammation of the testis) caused by mumps virus may cause **sterility**.





Mumps



- The diagnosis of typical cases usually can be made on the basis of **clinical** findings.
- Immunity is permanent after a single infection.
- An effective attenuated live-virus vaccine is available.
- Mumps vaccine is available in combination with measles and rubella (**MMR**) live-virus vaccines. **Two doses of MMR vaccine are recommended** for school entry.

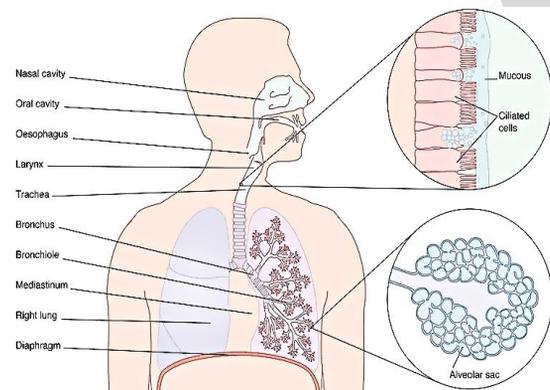
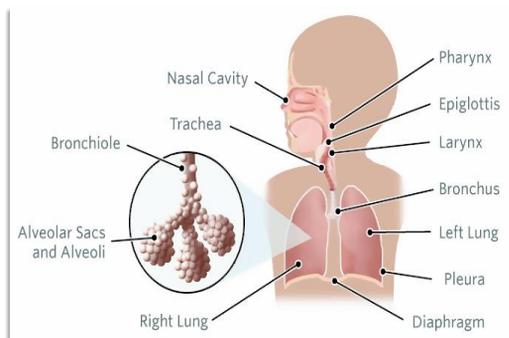




Parainfluenza viruses (PIVs 1-4)



Parainfluenza viruses are ubiquitous and cause common respiratory illnesses in persons of all ages. They are major pathogens of **severe** respiratory tract disease **in infants and young children**.

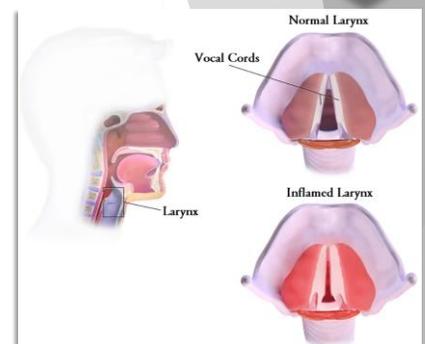




Parainfluenza viruses (PIVs 1-4)



- Parainfluenza virus replication in the immunocompetent host appears to be **limited to respiratory epithelia**.
- The infection may involve only the nose and throat, resulting in a harmless “**common cold**” syndrome.
- Infection may be more extensive and, especially with types 1 and 2, may involve the larynx and upper trachea, resulting in **croup** (**laryngotracheobronchitis**).





Parainfluenza viruses (PIVs 1-4)



- ❖ Factors that determine the severity of PIVs disease are unclear but include **both viral and host properties**, such as immune status of the patient, and airway hyperreactivity.
- ❖ Primary infection usually results in **rhinitis** and **pharyngitis**, often with **fever**. However, primary infections caused by PIV type 1, 2, or 3 can be serious ranging from **croup** (particularly with types 1 and 2) to **bronchiolitis** and **pneumonia** (particularly with type 3).
- ❖ **PIV type 4 does not cause serious disease.**
- ❖ The most common complication of PIVs infection is **otitis media**.



Respiratory Syncytial Virus (RSV)



- **RSV is the most important cause of lower respiratory tract illness in infants** and young children, usually outranking all other microbial pathogens as the cause of bronchiolitis and pneumonia in infants.
- Although the airways of very young infants are narrow and more readily obstructed by inflammation and edema, only a subset of young babies develops severe RSV disease.
- It has been reported that susceptibility to **bronchiolitis** is genetically linked to polymorphisms in innate immunity genes.



Respiratory Syncytial Virus (RSV)



- Children who have had RSV bronchiolitis and pneumonia as infants often exhibit recurrent episodes of wheezing illness for many years.
- RSV is an important cause of **otitis media**. It is estimated that 30–50% of wintertime episodes in infants may be caused by RSV infection.





Respiratory Syncytial Virus (RSV)



- Presumptive diagnosis of RSV infection in infants can often be made on the basis of the clinical syndrome combined with the time of year and other epidemiologic features.
- Radiographic findings are common but relatively nonspecific.
- Rapid detection is desirable to guide the use of appropriate infection-control measures and to potentially limit unnecessary antibiotic use.
- DFA and RT-PCR can be used for laboratory diagnosis.



Respiratory Syncytial Virus (RSV) Rx



- Treatment of serious RSV infections depends primarily on **supportive care** (e.g. removal of secretions, administration of oxygen).
- The antiviral drug **ribavirin** is approved for treatment of lower respiratory tract disease caused by RSV, especially in infants at high risk for severe disease.
- The drug is administered in an **aerosol** for 3–6 days.
- Monoclonal Ab (palivizumab) against RSV has been shown to reduce viral shedding.



Metapneumovirus infections



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ARTICLES

A newly discovered human pneumovirus isolated from young children with respiratory tract disease

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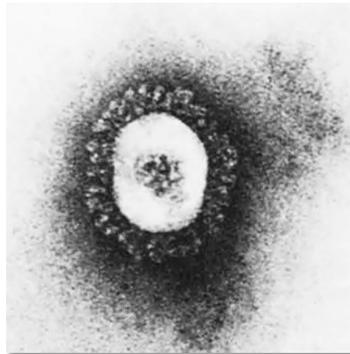
Metapneumovirus infections



- Human metapneumoviruses are associated with a variety of symptoms of the respiratory tract. These symptoms cannot be distinguished from those induced by RSV.
- Populations at risk besides children include elderly adults and immunocompromised individuals.
- Healthy adults tend to develop cold and flu-like symptoms in response to metapneumovirus infection. Asymptomatic infections are more common than for influenza virus or RSV in this population.
- There is no specific therapy for human metapneumovirus infections, and no vaccine is available.

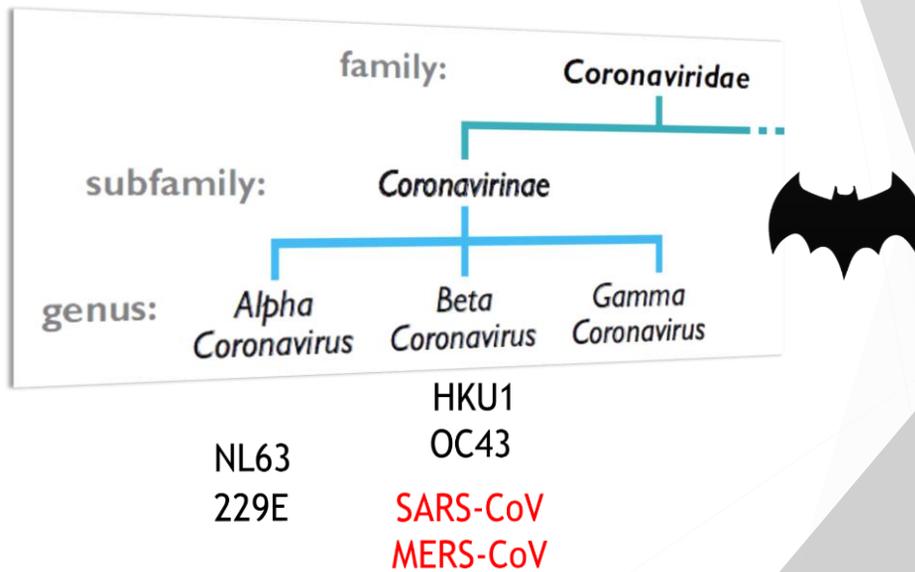


Coronaviridae



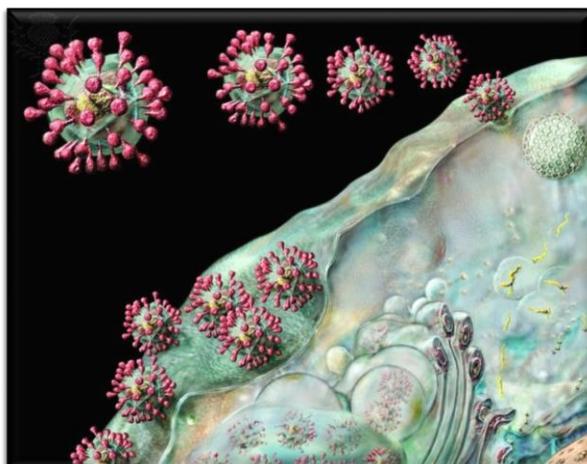


Coronaviridae Classification





Coronavirus Structure





Coronavirus Receptors



A



♥

SARS-CoV

NL63

Aminopeptidase N
(APN; CD13)

229E

Dipeptidyl
peptidase 4
(DPP4;CD26)

MERS-CoV

N-acetyl-9-O-
acetylneuraminic
acid

OC43

O-acetylated sialic
acid

HKU1



Coronavirus Transmission & Clinical Features





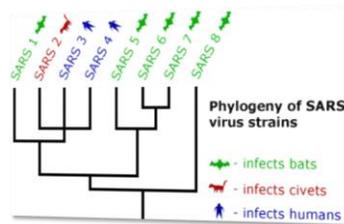
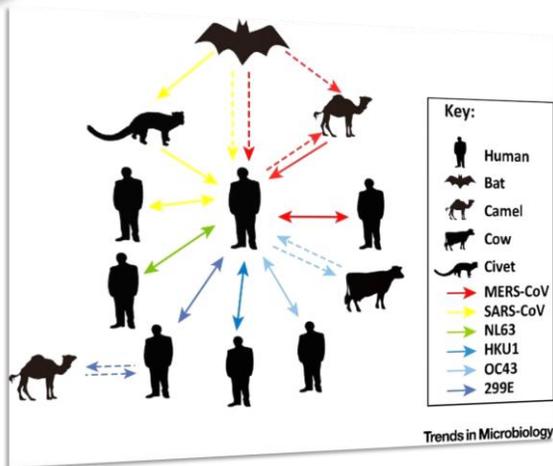
Clinical Features of Coronavirus Infections



HCoV	Clinical Symptoms	Case Fatality Rate	Incubation Period	Median Time to Death
229E	Coryza	N/A	2-5 days	-
OC43	Coryza	N/A	2-5 days	-
SARS-CoV	Fever, myalgia, headache, chills, cough, dyspnea, respiratory distress, diarrhea	9%	2-11 days	23 days
NL63	Coryza, Croup	N/A	2-4 days	-
HKU1	Coryza	N/A	2-4 days	-
MERS-CoV	Fever, myalgia, headache, chills, cough, dyspnea, pneumonia, vomiting, diarrhea	36%	2-13 days	14 days



Coronavirus Origin & Epidemiology





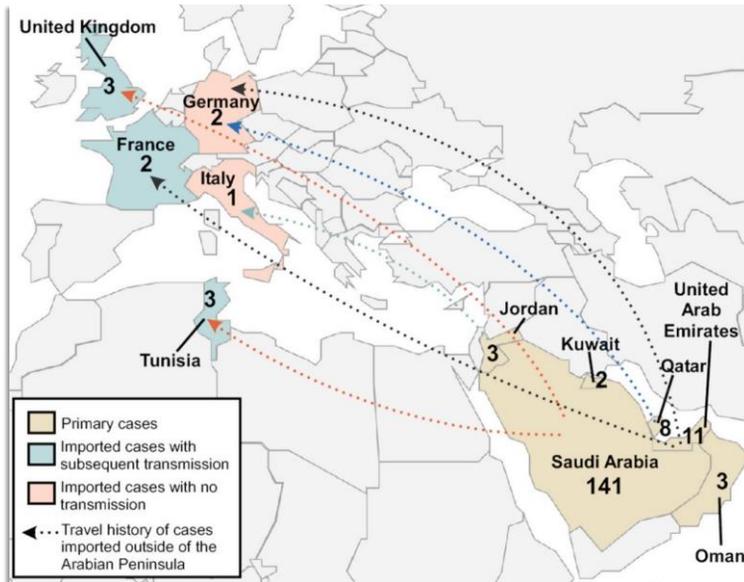
Coronavirus Origin & Epidemiology



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Coronavirus Origin & Epidemiology



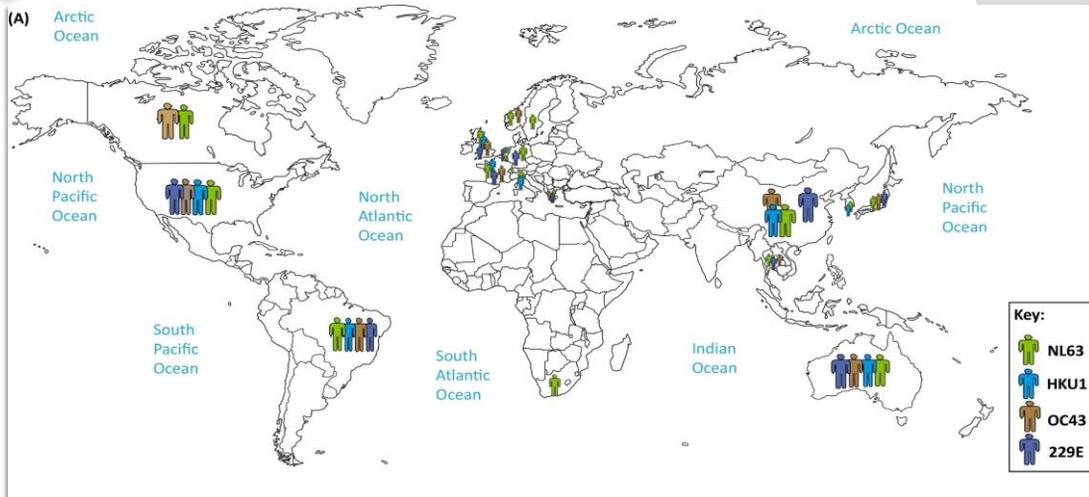


Coronavirus Origin & Epidemiology



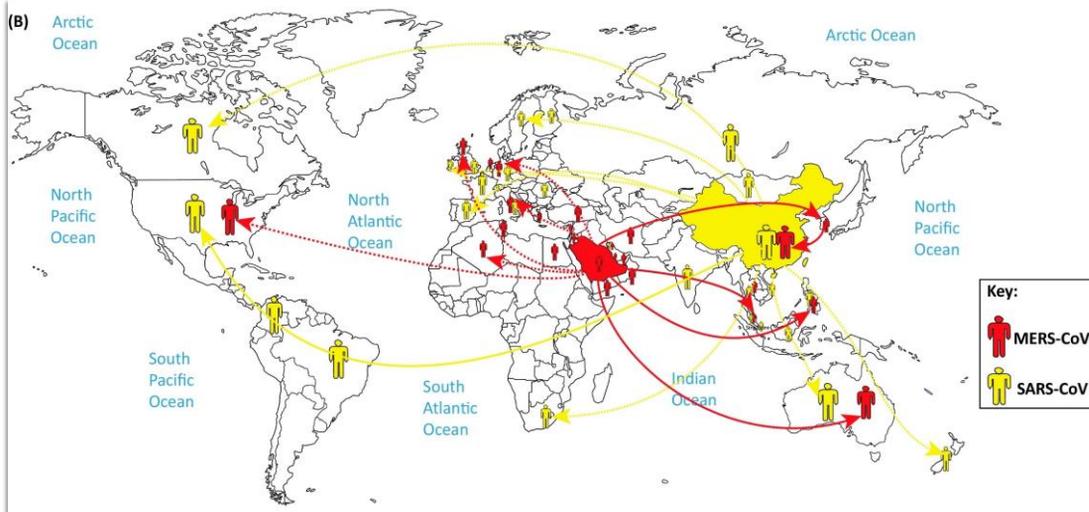


Coronavirus Origin & Epidemiology



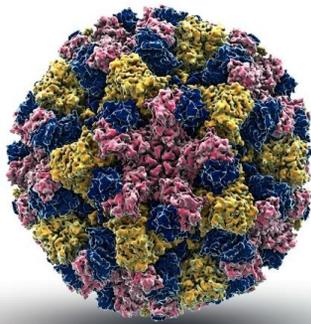


Coronavirus Origin & Epidemiology



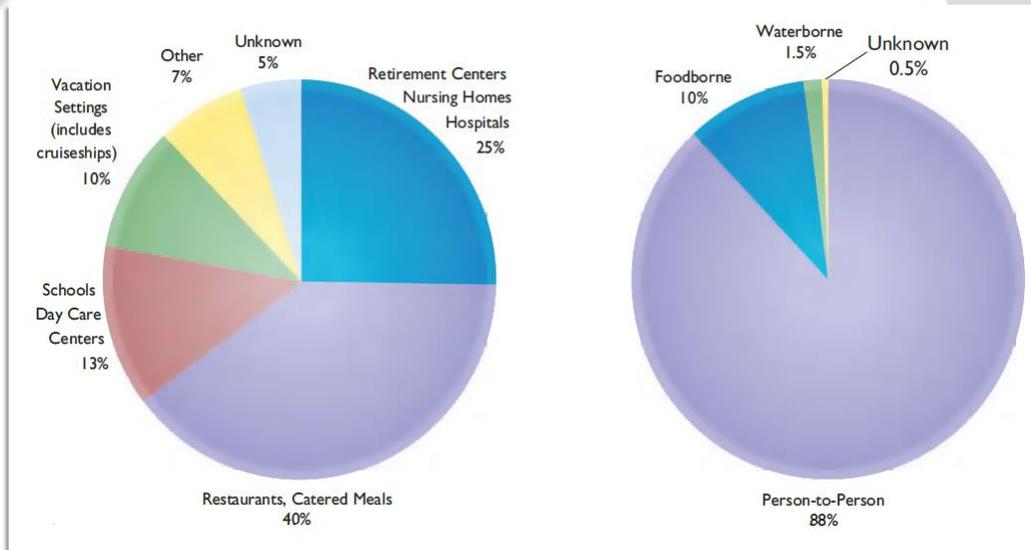


Caliciviridae





Norovirus Transmission



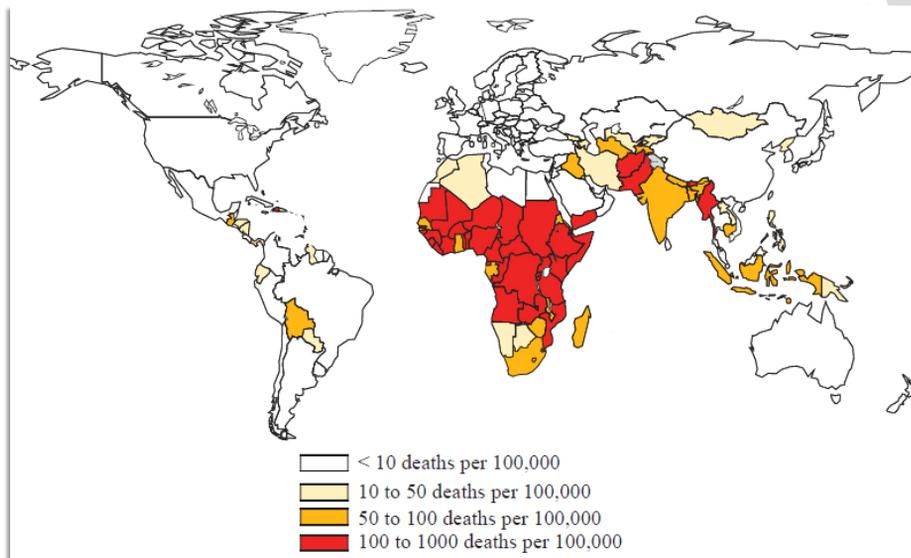


REOviridae



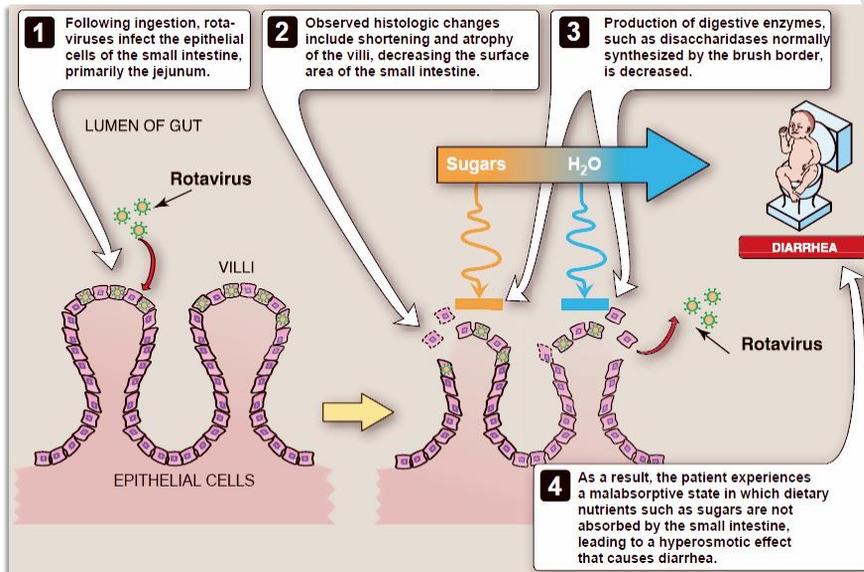


Rotavirus Gastroenteritis





Rotavirus Gastroenteritis





Rotavirus Dx, Rx and Prevention



Ready to use/ No reconstitution require

Oral suspension in pre-filled oral applicator

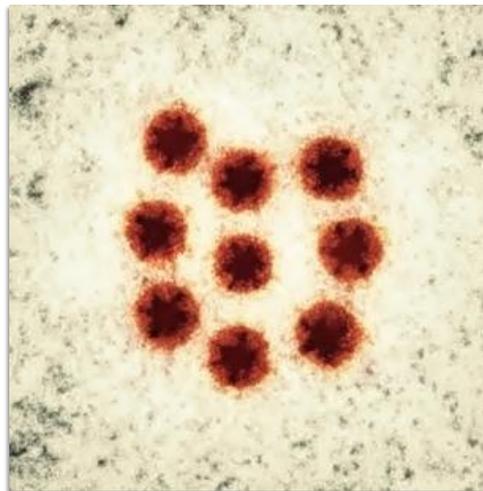
Rotarix®

Oral suspension in pre-filled oral applicator
Rotavirus vaccine, live
Oral use
Do not inject!

gsk GlaxoSmithKline



Astrovirus



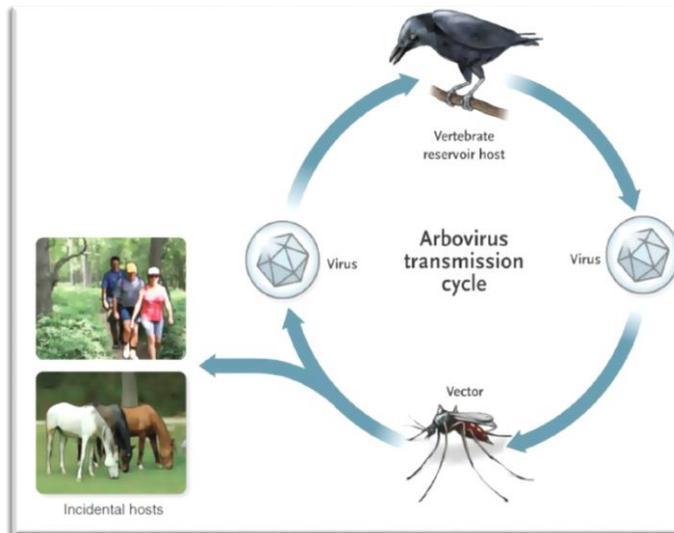


Introduction





Introduction





Arbovirus Replication



- The life cycle of the arboviruses is based on the ability of these viruses to multiply in both the **vertebrate host** and the **bloodsucking vector**.
- For effective transmission to occur, the virus must be present in the bloodstream of the vertebrate host (viremia) in sufficiently high titer to be taken up in the small volume of blood ingested during an insect bite.





Arbovirus Replication



- After ingestion, the virus replicates in the gut of the arthropod and then spreads to other organs, including the **salivary glands**.
- Only **the female** of the species serves as the vector of the virus, because only she requires a blood meal in order for progeny to be produced.



Arbovirus Replication



- Usually, humans are **dead-end hosts**, because the concentration of virus in human blood is *too low* and the duration of viremia is *too brief* for the next bite to transmit the virus.



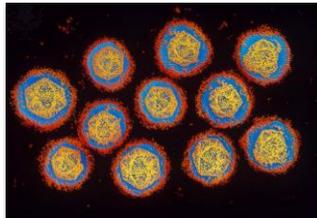
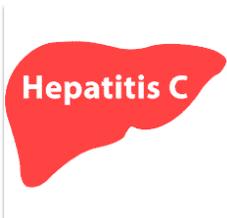


Togaviridae (Alphavirus)





Flaviviridae





Dengue Fever



- Dengue (**breakbone fever**) is a mosquito-borne infection that is characterized by fever, severe headache, muscle and joint pain, nausea and vomiting, eye pain, and rash.
- Dengue is endemic in more than 100 countries and is considered the most prevalent of all arboviruses in humans.
- Control depends on antimosquito measures.

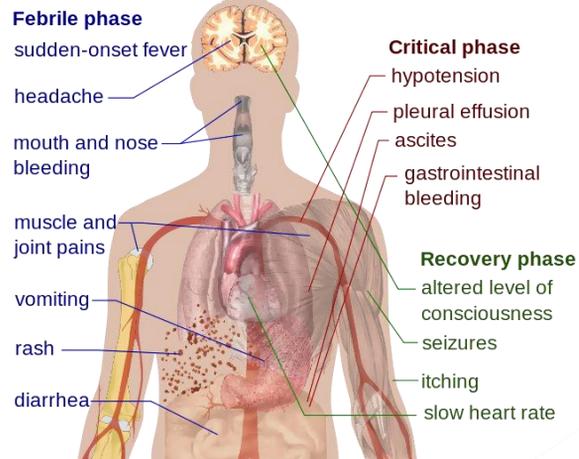
حمى الضنك



Dengue Fever

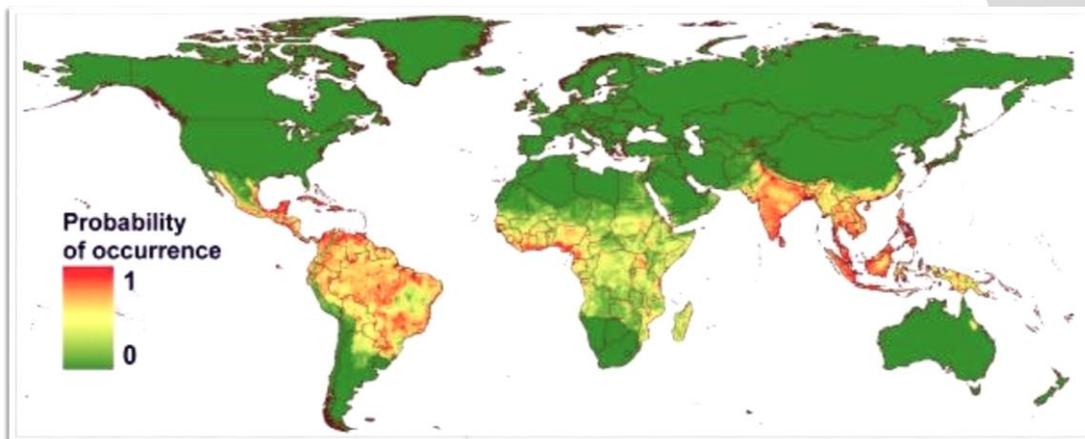


Symptoms of Dengue fever





Dengue Fever Epidemiology





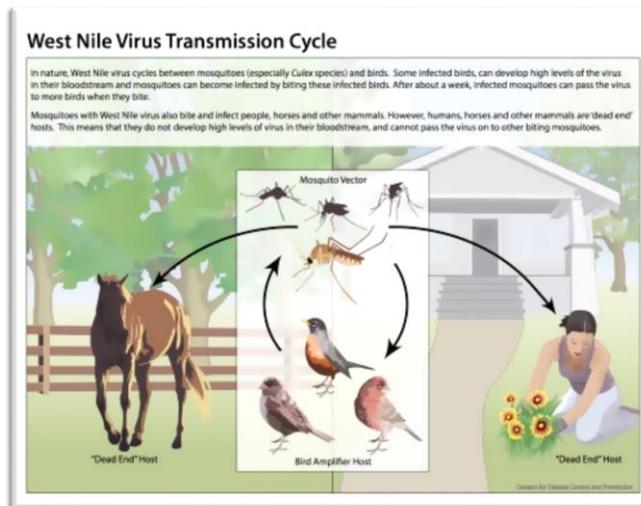
West Nile Fever (WNF)



- It occurs in Europe, the Middle East, Africa, the former Soviet Union, Southwest Asia, and, more recently, the United States.
- It appeared unexpectedly in the New York City area in 1999, resulting in seven deaths and extensive mortality in a range of domestic and exotic **birds**.



West Nile Fever (WNF)





West Nile Fever (WNF)



- Sequence analysis of virus isolates showed that it originated in **the Middle East**; it probably crossed the Atlantic in an infected bird, mosquito, or human traveler.
- About 80% of West Nile infections are **asymptomatic**, with about 20% causing **West Nile fever** (fever, headache, skin rash, and LAP) and less than 1% causing **neuro-invasive disease** (meningitis, encephalitis).



Zika Fever



- Zika virus is transmitted by mosquitoes.
- Other non-vector modes of Zika virus transmission include **congenital** and sexual.
- Infection is likely asymptomatic in about 80% of cases.
- When symptoms occur, they are typically mild, self-limiting, and nonspecific.



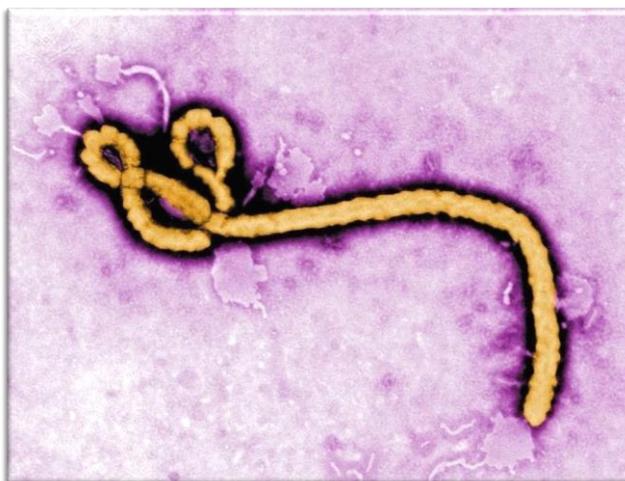
Zika Fever



- Commonly reported symptoms include rash, fever, arthralgia, myalgia, fatigue, headache, and conjunctivitis
- Rash, a prominent feature, is maculopapular and pruritic in most cases.
- Spontaneous resolution within 1–4 days of onset.
- Congenital infection association with microcephaly?

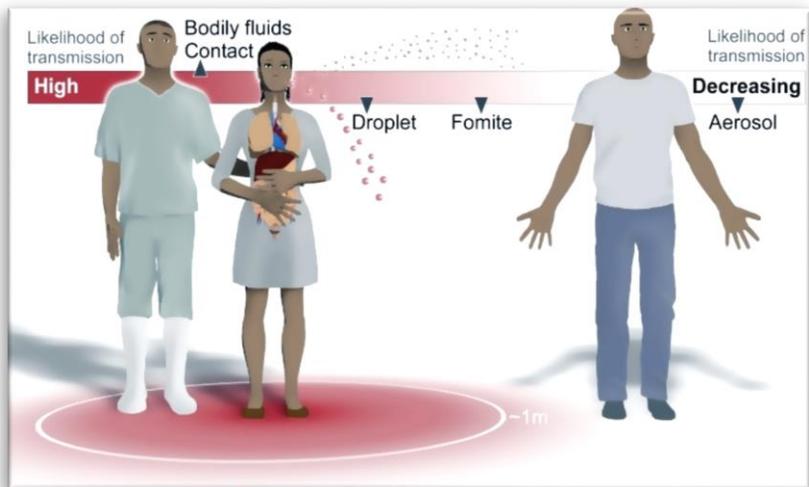


Ebola





Ebola Transmission





Ebola



- Characterized by fever, headache, sore throat, and myalgia followed by abdominal pain, vomiting, diarrhea, and rash, with both internal and external bleeding, often leading to shock and death.
- Ebola virus has a tropism for cells of the macrophage system, dendritic cells, interstitial fibroblasts, and endothelial cells.



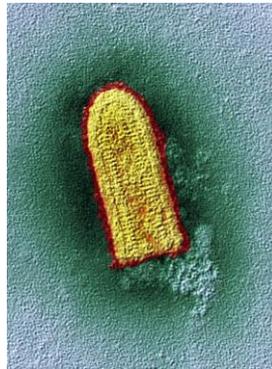
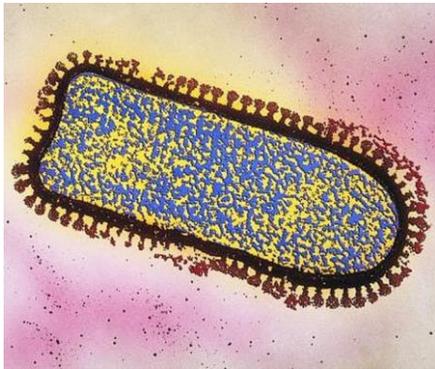
Ebola



- Very high titers of virus are present in many tissues, including the liver, spleen, lungs, and kidneys, and in blood and other fluids.
- Filoviruses have the highest mortality rates of all the viral hemorrhagic fevers.



Rabies Virus Description



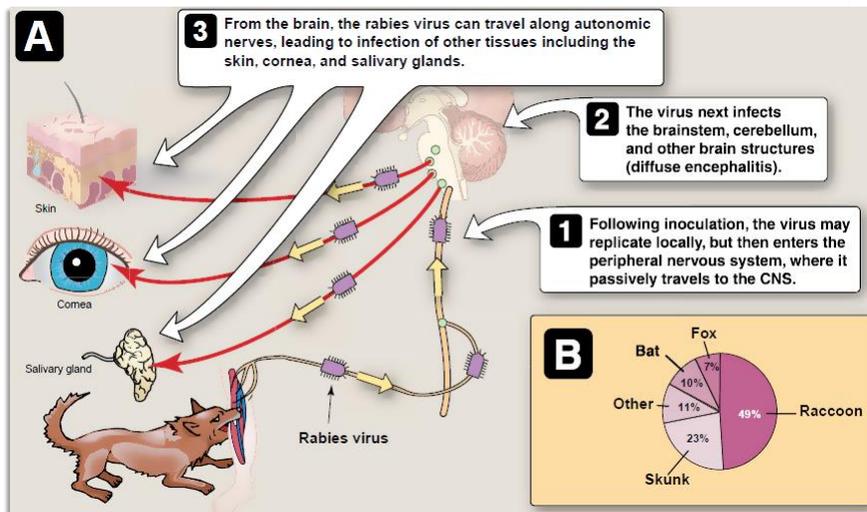


Animal Susceptibility





Rabies Pathogenesis and Pathology





Rabies Pathogenesis and Pathology



- Rabies virus multiplies in muscle at the site of inoculation and then enters peripheral nerves at NMJs and spreads up the nerves to the CNS.
- The virus multiplies in the CNS and progressive **encephalitis** develops.
- The virus then spreads through peripheral nerves to the salivary glands and other tissues.
- **The organs with the highest titers of virus are the salivary gland.** Other organs where rabies virus has been found include pancreas, kidney, heart, retina, and cornea.



Rabies Pathogenesis and Pathology



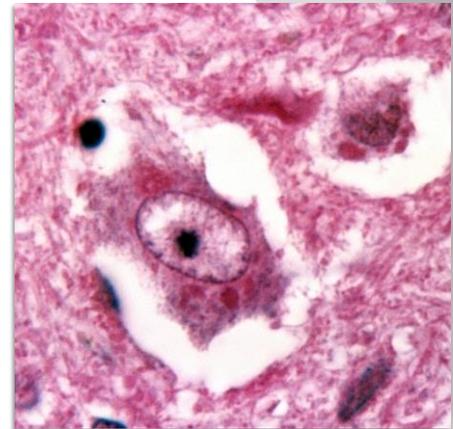
- The incubation period (typically 1–3 months but **may vary from 1 week to 1 year**) depends on the host's age, genetics, and immune status, the **viral strain**, **amount of inoculum**, the **severity of lacerations**, and the **distance the virus has to travel** from its point of entry to the CNS.
- There is a higher attack rate and shorter incubation period in persons bitten on the face or head; the lowest mortality occurs in those bitten on the legs.



Rabies Pathogenesis and Pathology



- Rabies virus produces a specific **eosinophilic cytoplasmic inclusion**, **the Negri body**, in infected nerve cells, that are filled with viral nucleocapsids.
- **The presence of such inclusions is pathognomonic of rabies** but is not observed in at least 20% of cases.





Rabies Clinical Features



- The clinical spectrum can be divided into three phases:
 - **Prodrome:** malaise, anorexia, headache, photophobia, nausea and vomiting, sore throat, and fever.
 - **Acute neurologic phase:** CNS signs including nervousness, apprehension, hallucinations, and bizarre behavior. sympathetic overactivity is observed, including lacrimation, pupillary dilatation, and increased salivation and perspiration. Hydrophobia and aerophobia are common as well.
 - **Coma and death:** The major cause of death is cardiorespiratory arrest.



Rabies Diagnosis



- Clinical through history of exposure.
- Rabies antigens or nucleic acid detection.
- Serology.
- Virus isolation.



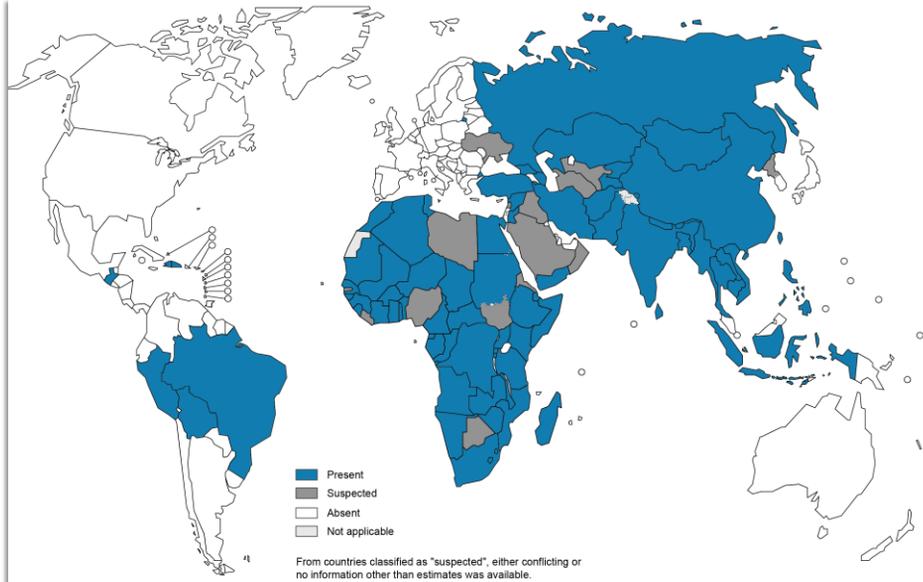
Rabies Management



- Once an individual has clinical symptoms of rabies, there is no effective treatment.
- A killed rabies virus vaccine is available for prophylaxis.
- Postexposure prophylaxis refers to treatment after an animal bite or suspected of being rabid, and consists of thorough **cleaning of the wound, passive immunization, and active immunization.**
- Prevention of initial exposure is, however, the most important mechanism for controlling human rabies.



Rabies Epidemiology





Transmissible Spongiform Encephalopathies (Prion Diseases)





Transmissible Spongiform Encephalopathies (Prion Diseases)



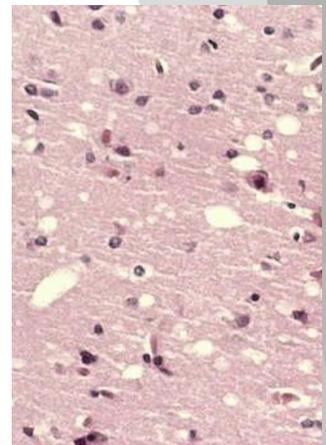
- Transmissible spongiform encephalopathies are **degenerative CNS diseases**.
- Infectivity is associated with **proteinaceous material devoid of detectable amounts of nucleic acid**.
- Prions are resistant to treatment with formaldehyde, dry heat, boiling, ethanol, proteases, and ionizing radiation.
- Prions are sensitive to phenol, household bleach, ether and autoclaving (1 hour, 121°C). Guanidine thiocyanate is highly effective in decontaminating medical supplies and instruments.



Prion Diseases



- Prion diseases are **confined to the nervous system**.
- The basic features are **neurodegeneration and spongiform changes**.
- Long incubation periods (months to decades) precede the onset of clinical illness and are followed by chronic progressive disease (weeks to years).
- The diseases are always fatal, with no known cases of remission or recovery.

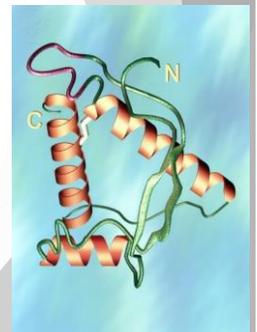




Prion Diseases



- PrP^C Protein (encoded by a chromosomal gene, designated PRNP in humans)
- The PrP gene is located on the short arm of chromosome 20 in humans.
- In contrast to viruses, **prions are non-immunogenic**.
- The crossing of prions from one species to another is restricted by what has been called the “species barrier”.
- The prion diseases are uniformly fatal. No human or animal has ever recovered from a prion disease once neurologic dysfunction is manifest.

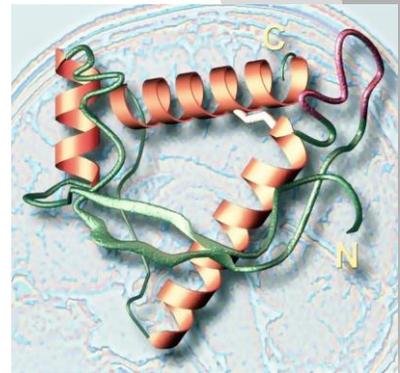




Transmissible Spongiform Encephalopathies (Prion Diseases)



- Prions are composed entirely of protein.
- It is proposed that PrP^{Sc} acts as a template which promotes the conversion of PrP^C to PrP^{Sc} and that this conversion involves **only conformational change**.
- In humans, the PrP prion diseases occur in three different forms: (a) sporadic, (b) inherited, and (c) infectious





Kuru and Creutzfeldt–Jakob Disease



- CJD is a progressive multifocal dementia, peak onset between 60–65.
- Kuru occurred only in the eastern highlands of New Guinea and was spread by customs surrounding **ritual cannibalism** of dead relatives. Since the practice has ceased, the disease has disappeared.
- CJD in humans develops gradually, with progressive dementia, ataxia, and myoclonus, and leads to death in 5–12 months.



BSE and vCJD



- A disease similar to scrapie, designated bovine spongiform encephalopathy (BSE), or “mad cow disease,” emerged in cattle in Great Britain in 1986.
- This outbreak was traced to the use of cattle feed that contained contaminated bone meal from scrapie-infected sheep and BSE-infected cattle carcasses.
- The use of such cattle feed was prohibited in 1988. The epidemic of “mad cow disease” peaked in Great Britain in 1993.



BSE and vCJD



- In 1996, a new variant form of CJD was recognized in the United Kingdom that occurred in younger people and had distinctive pathologic characteristics similar to those of BSE.
- It is now accepted that the new variant forms of CJD and BSE are caused by a common agent, indicating that the BSE agent had infected humans.
- Through 2006, over 150 people had been diagnosed with new variant CJD in England, and most had died.



Thanks!
Wishing YOU ALL the Best of Luck
I will miss you all :’(