

Viruses **from the Deadliest to Beneficial**

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Theories of Viral Evolution

- 1. Viruses are thought to have evolved from either the DNA or RNA of host cell that developed the ability to replicate autonomously.
- 2. Another thought is that viruses could be degenerate forms of intracellular parasites.

Viral Strains Differ Greatly

- Genome organization
- Structure
- Expression
- Replication
- Transmission

- Viruses can infect:
- Humans
- Animals
- Plants
- Single-cell organisms including mycoplasma, bacteria & algae

The Deadliest Viruses on Earth

Marburg Virus

Hantaviruses

Lassa Fever Virus

HIV

Influenza

Rotavirus

SARS-COV

COVID-19

Ebola Virus

Japanese Encephalitis Virus

Rabies

Smallpox

Dengue

Polio Virus

MERS-COV

MARBURG VIRUS

1967 in Marburg, Germany

1998-2000 Democratic Republic Congo

2005 Angola

- Marburg Virus is a member of the Filovirus family causing hemorrhagic fever (~ to Ebola)
- Origin : Green Monkeys endemic to Uganda; Bats are thought to be a natural reservoir
- Symptoms: fever, headache, sore throat, myalgias, arthralgias, epigastric pain, vomiting, diarrhea
- Death Rate 25% in '67, 80% '98-2005 by bleeding into gastrointestinal tract, skin, disseminated intravascular coagulation, shock, multi-organ failure
- No Treatment, No Anti-viral
- No Vaccine



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EBOLA VIRUS

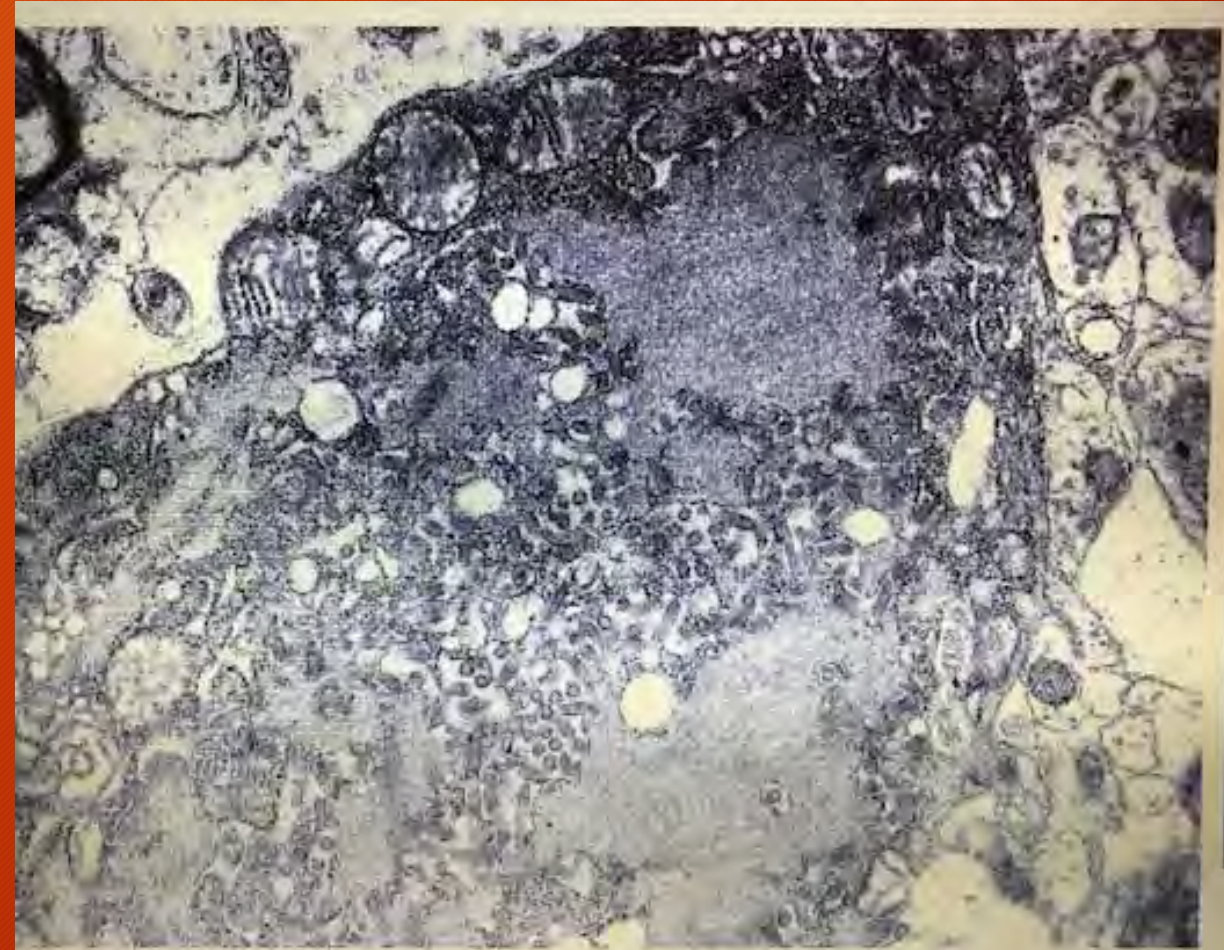
1976 in Sudan & Democratic Republic of Congo
2014-2016 West Africa

- Origin: uncertain; thought to originate in fruit bats and transmitted to other animals
- Transmission: through blood, body fluids and infected tissues from humans and animals
- Death rate varies with strains: 71% Sudan strain, 50% Bundibugyo strain
- 2014 WHO: largest outbreak and most complex ~ 11,000 of infected died
- Symptoms: fever, fatigue, muscle pain, headache, sore throat, vomiting, diarrhea, rash, impaired liver and kidney function, internal and external bleeding
- No Anti-viral
- Antibody Treatment tried
- Ongoing efforts to make a vaccine



RABIES 1920

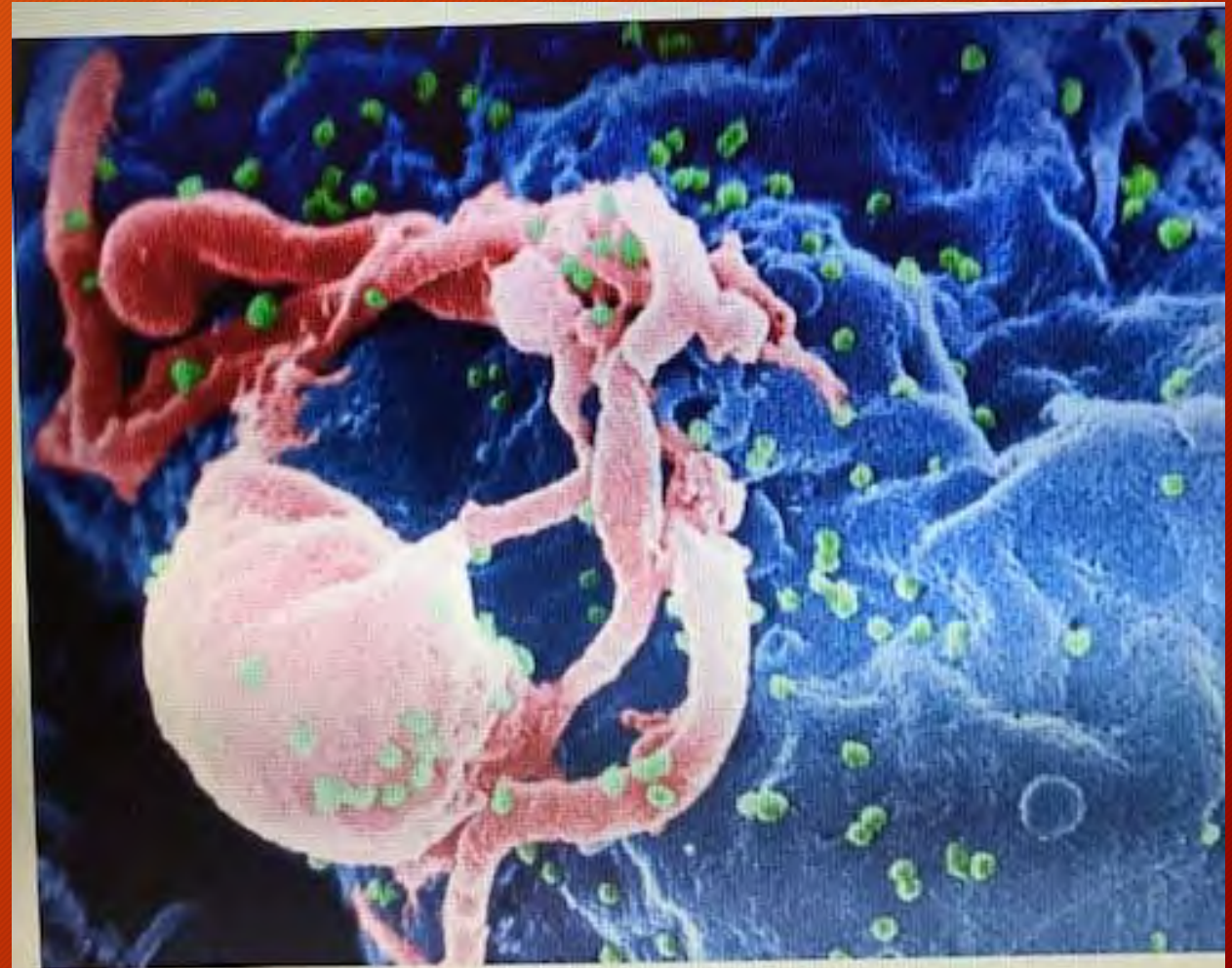
- Rabies is found in 150 countries world-wide causing tens of thousands of deaths/yr mostly in Africa & India
- Caused most frequently by dog bites and bat bites. Wild animals also carry and transmit Rabies Virus
- Incubation period is 2-3 months
- 2 Types: Furious Rabies and Paralytic Rabies
- Most frequent victims are children ages 5-14 years.
- Symptoms: fever, pain, tingling, pricking or paresthesia at wound site.
- As Virus progresses into the central nervous system, fatal inflammation and destruction of brain and spinal cord causing altered mentation, behavior, coma, cardiorespiratory arrest and death.
- 100% Death if NOT treated with antibodies
- Vaccine developed for pets in 1920's



(Image credit: CDC/ Dr. Fred Murphy)

HIV Human Immunodeficiency Virus 1980's

- The deadliest virus in the Modern World causing over 3.1 Million Deaths yearly
- Still devastates in lower and middle-income countries where 95% cases occur
- WHO African Region estimates 1/25 adults is HIV Positive accounting for 25.5 Million people with HIV world-wide
- HIV is Enveloped positive-strand RNA virus in Retroviridae family
- Transmission: sexual contact, blood,, organ/ tissue transplantation
- Symptoms usually begin within 10 days of infection, fever, rash arthralgias, myalgias, malaise, lymphadenopathy, oral ulcers, pharyngitis, weight loss
- Rx: Anti-viral agents in combination therapy



(Image credit: Cynthia Goldsmith, Centers for Disease Control and Prevention)

SMALLPOX VIRUS

Existed for Thousands of Years, Eradicated 1980

- Caused by variola virus of genus Orthopoxvirus
- Person to person spread by respiratory secretions or contact with infectious skin lesions. Animal to human spread by contact with infected animals.
- Incubation 7-19 days
- Symptoms: fever, rash progressing deep seated pustular lesions
- Treatment antiviral & supportive care, covering wounds
- 90% of Native population of the Americas died from smallpox brought by European explorers.
- In 20th century, ~ 300 million people died from smallpox
- Intensive vaccination program helped eradicate Smallpox by 1980 Last case 1977
- This is the First Viral Infection to be Eradicated - WHO declared 1980



HANTAVIRUS 1950's Korean War and 1993 in New Mexico & Arizona

- Hantavirus is an enveloped RNA virus in the family of Bunyaviruses causing viral hemorrhagic fever with renal syndrome and hantavirus pulmonary syndrome
- Infected by contact with deer mouse urine / feces or saliva in bite
- Incubation time up to 21 days
- Symptoms: fever, myalgias, headache, petechial rash, vomiting, diarrhea, fatigue, then 4-10 days later cough, shortness of breath pulmonary edema, acute respiratory distress syndrome
- In 1950's during Korean War >3,000 troops infected Mortality 12%
- In 1993 > 600 people infected and Mortality 36%
- No Treatment, Cure or Vaccine

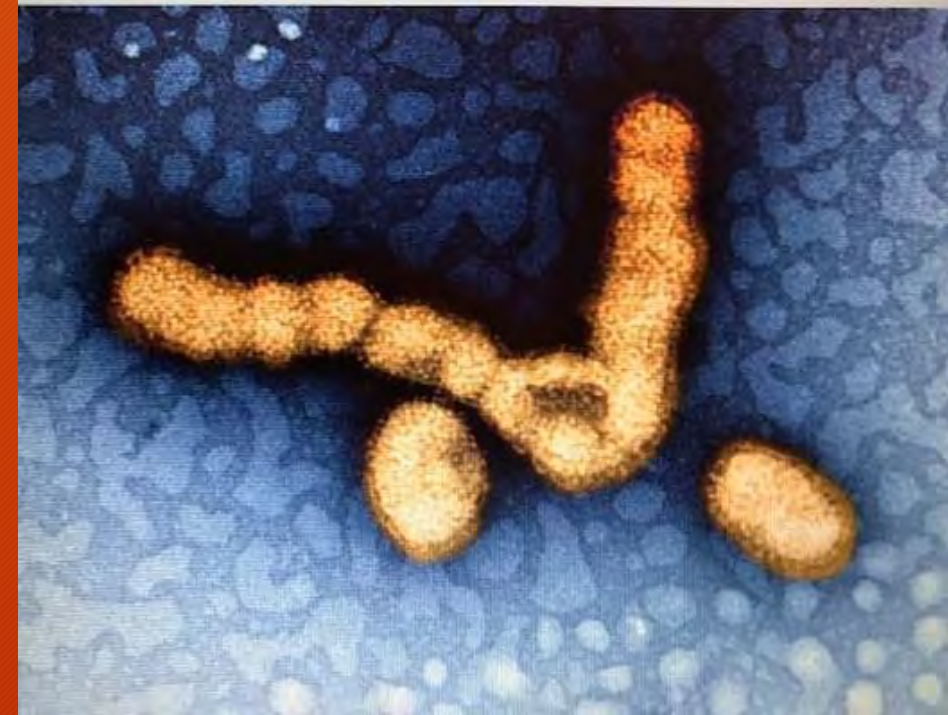


credit: Cynthia Goldsmith. Provided by CDC/ Brian W.J. Mahy, PhD; Luanne H. Elliott, M.S.)

INFLUENZA VIRUS

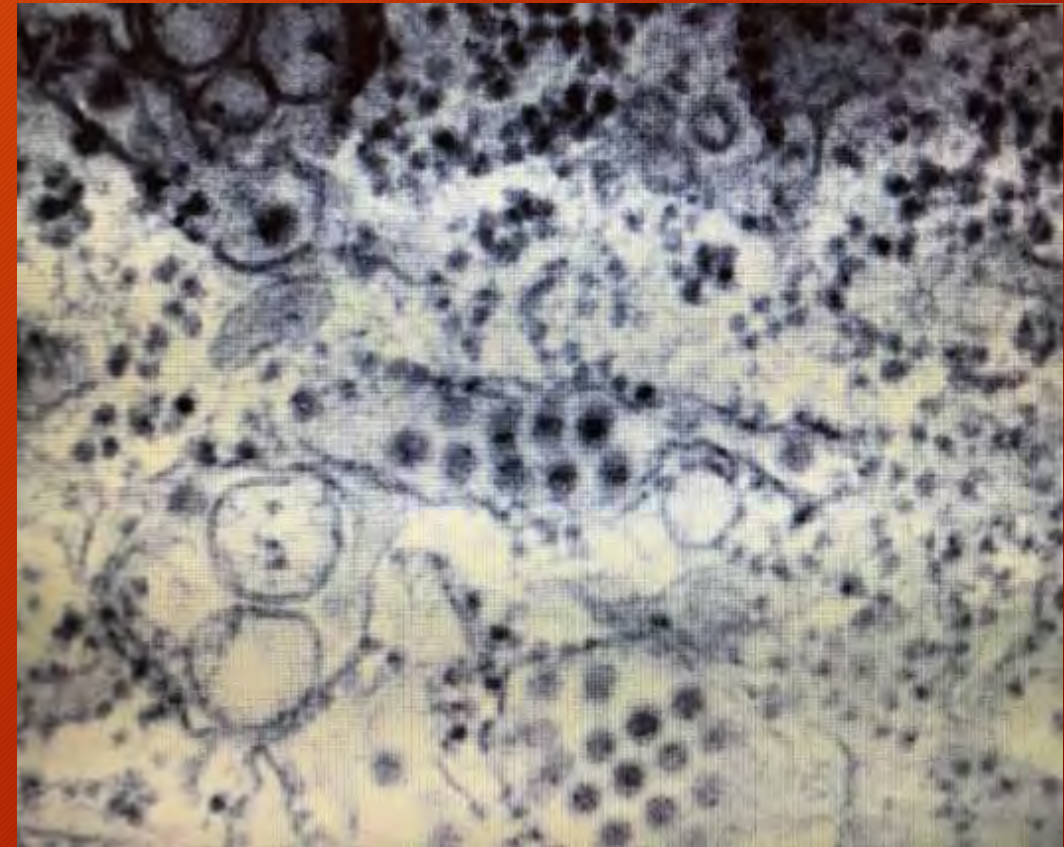
World's Single Biggest Killer 1918

- Influenza viruses are RNA viruses of the Orthomyxovirus genus.
- There are 4 Types: A,B,C,D - A(H1N1), A (H3N2), B-Yamagata, B-Victoria viruses cocirculate in humans worldwide with the distribution varying year to year and between geographic areas
- Avian influenza A(H5N1) & A(h7N9) and swine- origin A(H1N1), A(H1N2) & A (H3N2) variants have led to sporadic Human infections
- Transmission is respiratory droplet inhalation or touching contaminated surfaces then touching face. More prevalent in colder months.
- Humans can spread virus from day before onset & up to 5-10 + days after onset of symptoms
- Severity of illness and death rate increases with age ≥ 65 and <2 years & immunocompromised
- Symptoms: fever, myalgias, headaches, non-productive cough, sore throat, rhinitis, vomiting
- Anti-viral agents, Vaccines
- 1918 Most Deadly Spanish Flu sickened half a billion people (40% world population) killing 50 -100 Million people (5% of planet's population)
- IN USA, CDC estimates 9.2-35.6 Million infected with flu and 12,000-56,000 deaths A(H1N1) strain is most lethal with 20% mortality



DENGUE 1950's in Philippines & Thailand

- Dengue first appeared in 1950's in Philippines and Thailand spreading to tropical and subtropical regions carried by *Aedes* mosquitoes
- Acute febrile illness caused by any of 4 related positive-sense, single stranded RNA viruses of the genus *Flavivirus*, dengue virus 1,2,3,4
- Generally 7 day Viremia in humans so contact with blood, tissue & organs of infected persons possible
- Symptoms: fever, nausea, vomiting, rash, myalgias, arthralgias, petechial hemorrhages, mucosal bleeding, abdominal pain, edema, lethargy, low BP, shock, respiratory distress, severe bleeding, enlarged liver, elevated liver tests
- Causes Dengue Hemorrhagic Fever with 20% mortality if left untreated.
- Now affects 50-100 Million people/year Most prevalent in Latin America, Caribbean and Southeast Asia but occurs in > 100 countries
- Mortality Rate 2.5%
- Vaccine just approved in 2019 for children 9-16 yrs in endemic areas. Other vaccines have been tried in some countries in 9-45 yr olds if they have had a confirmed case of Dengue in past. If no previous Dengue infection, the vaccine could cause a severe case of Dengue.



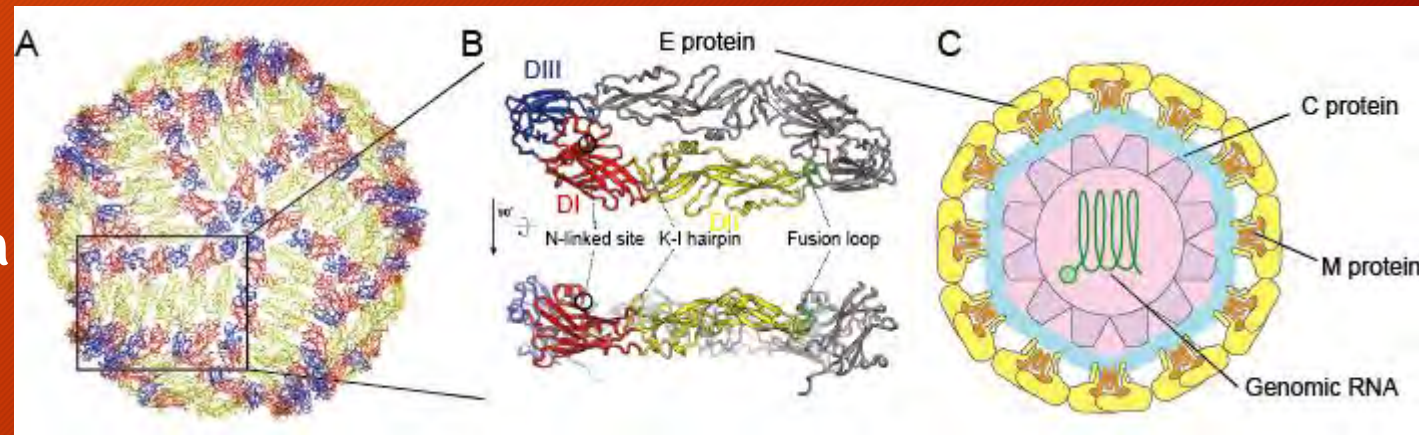
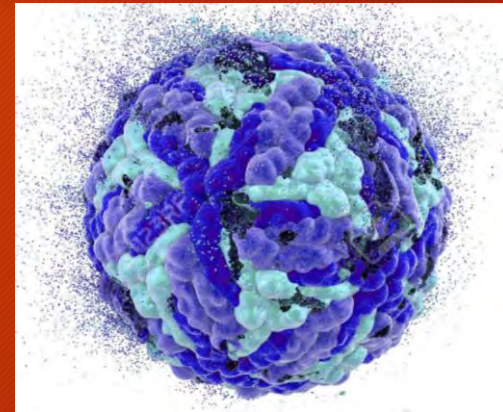
ROTAVIRUS

- Rotavirus is in genus of double stranded RNA virus in the family of Reoviridae
- Causes severe diarrhea in babies and children
- Transmission: fecal-oral route
- High death rate in developing world where rehydration treatment with fluids not available
- In 2008, 453,00 children < 5 years died
- 2 Vaccines are now available for children



Japanese Encephalitis Virus

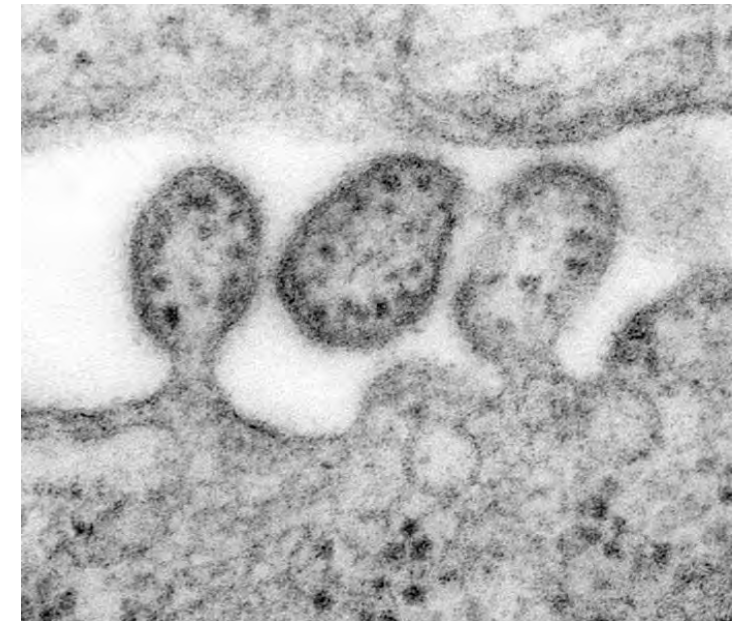
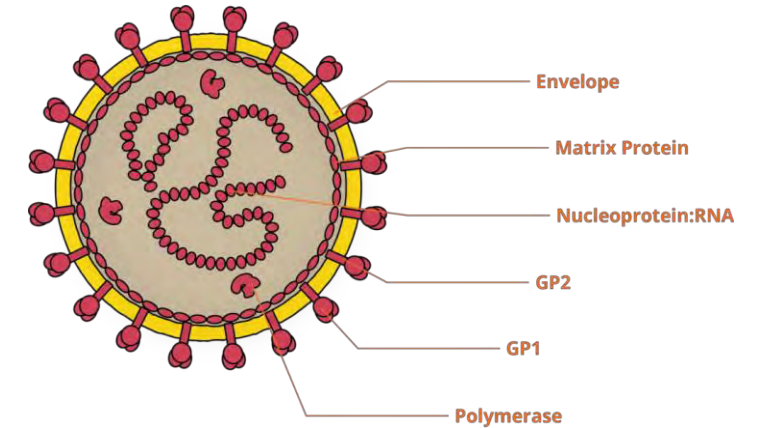
- WHO says 24 countries in South & East Asia and Western Pacific have endemic Japanese Encephalitis Virus putting over 3 Billion people at risk spread by mosquitoes of Culex species in rice fields; birds & pigs are reservoirs
- Generally 68,000 clinical cases / year
- Symptoms fever, neck rigidity, altered consciousness, headache, tremor, incoordination, seizures
- Death rate 30%
- 30-50% of Survivors have serious neurological and psychological sequela
- Vaccine available
- No antiviral treatment available



LASSA FEVER VIRUS

1969 Lassa Nigeria

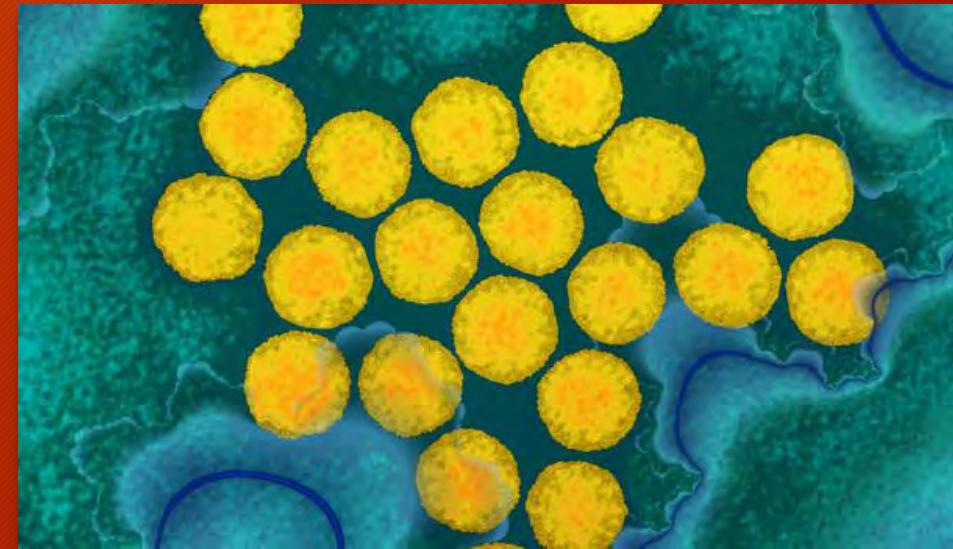
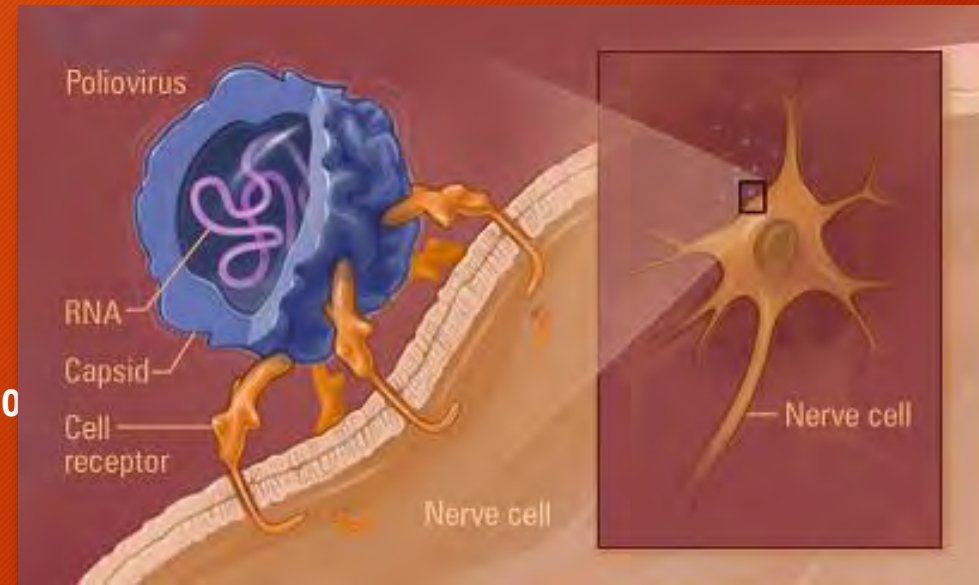
- **Lassa virus is an enveloped RNA virus in the family of Arenaviruses causing hemorrhagic fevers with reservoir host species are rats and mice**
- **Lassa virus is in the category Old World Arenaviruses (eastern hemisphere) occurring across rural west Africa with hyperendemic areas in parts of Sierra Leone, Guinea, Liberia, and Nigeria**
- **Transmission is by direct contact with symptomatic patient, body fluids, cadavers, inhalation of rodent urine aerosols, ingestion of rodent contaminated food, contact with infected rodents.**
- **Symptoms: fever, myalgias, headaches, petechial rash, ecchymoses, severe bleeding, vomiting, diarrhea, abdominal pain, shock, pulmonary edema and liver injury., spontaneous abortions and birth defects.**
- **Treatment: Ribavirin in addition to supportive care. Hyperimmune serum derived from survivors is saved for very severe cases.**
- **No Vaccine**
- **Mortality 15 - 50%**



POLIOVIRUS

Existed since 1400BCE by Egyptian sources,
1894 1st Epidemic in Vermont

- Polio viruses small non-enveloped viruses with a single-stranded RNA genome genus Enterovirus, serotypes 1,2,3, inactivated by heat. Virus identified 1908.
- Polio Epidemics only known since the 20th century. 1916 Polio epidemic in New York City Peak incidence. In 1952 another epidemic in US 58,000 cases with 3,000 deaths
- Transmission: person to person by oral & fecal-oral routes. Virus viable in nasopharyngeal secretions for 1-2 weeks and stool for 3-6 weeks
- Symptoms: sore throat, fever, tiredness, nausea, headache, stomach pain, paresthesias(pins& needle), meningitis 1/25, paralysis 1/200, 2-10 of 100 with paralysis die because virus affects respiratory muscles.
- Postpolio Syndrome: worsening of weakness or paralysis 20-30 years after original infection
- No Anti-viral treatment
- 1955: Polio Vaccine Inactivated IVP by Salk and then live oral polio vaccine in 1960's by Sabin
- Last case of Polio in US 1979 and in the Americas I 1991
- WPV Type 2 last seen 1999, WHO declared eradicated 2015, Last WPV Type 3 was 2012
- Currently 2019 there were 173 cases WPV Type 1 in Pakistan & Afghanistan
- Circulating vaccine derived poliovirus, cVDPV, has occurred necessitating reformulation of the oral polio vaccine



SARS-COV - Severe Acute Respiratory Syndrome Coronavirus

- **RECENT DISCOVERIES OF HUMAN CORONAVIRUSES**
- **2002-3 SARS-CoV – Severe Acute Respiratory Syndrome**
- **Started in Guangdong province, China. Thought to originate in bats then spread to animals then man but not confirmed. Infected 8,000 & caused 770 deaths Mortality 9.6%**
- **Symptoms: fever, chills, body aches, often progressed to pneumonia in which lungs become inflamed and filled with pus.**
- **Older adults with Diabetes, heart disease, immune compromised, lung disease, cancer higher risk & mortality**
- **No proven effective Treatment or vaccine**
- **No new cases since 2004**
- **Genome: deletion of 29-nucleotide sequence of the Coronavirus**

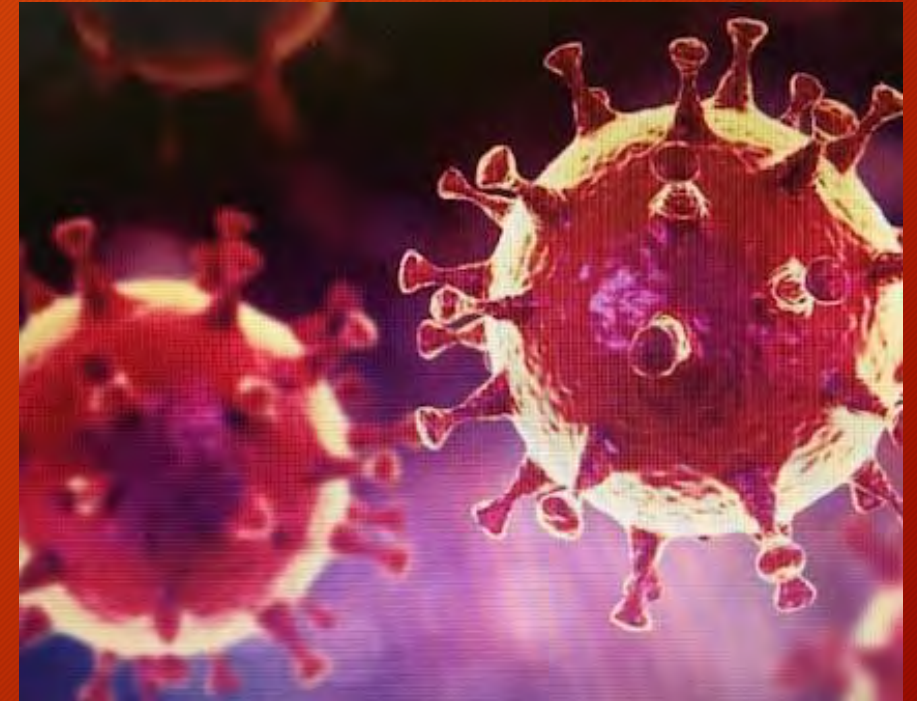


MERS - Middle East Respiratory Syndrome

- Most Lethal Coronavirus - MERS
- **2012 – present MERS – Middle East Respiratory Syndrome**
- **Started in Saudi Arabia origin unknown, possible bats with transmission through camels**

2015 outbreak in South Korea origin unknown

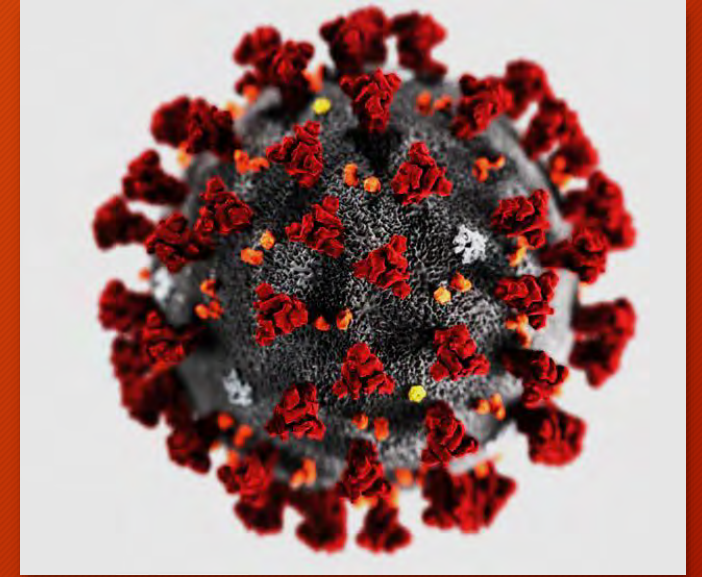
- **2,500 cases in 27 countries & 860 deaths Mortality 30-40%**
- **Older adults with Diabetes, heart disease, immune compromised, lung disease, cancer have higher risk & mortality**
- **Symptoms: fever, cough, shortness of breath, pneumonia**
- **No proven effective Treatment or Vaccine**



COVID-19

Novel Coronavirus 2019

- **First Identified December 2019 in Wuhan, Hubei Province, China Population 14 Million**
- **Initially, 99 patients – 67 Males, 32 Females with pneumonia; 51% had chronic diseases; 49% had exposure in Huanon Seafood Market**
- **Symptoms: Fever 82%, Cough 82%, Shortness of Breath 31% Confusion 9%, Headache 8%, Sore throat 5%, Rhinorrhea 4% Chest pain 2% Diarrhea 2% Nausea & vomiting 1%**
- **Complications: 74% Bilateral Pneumonia, multiple mottled and “ground glass” opacities**
- **17% Acute Respiratory Distress Syndrome (similar to SARS)**
- **11% Died of Multi Organ Failure**
- **WITHIN 3 MONTHS COVID-19 has spread to 170 countries and infected 207,000 people and caused 8,500 deaths**
- **At Risk: Elderly and those with underlying conditions: Diabetes, lung, heart & Kidney disease, Immunocompromised children and adults at higher risks for pneumonia and respiratory failure syndrome and death**
- **No specific treatment yet**
- **No Vaccine Yet**



Beneficial Viruses

1. Oncolytic Viral Therapy:

- Certain viruses may have potential use in curing cancers such as :Hepatocellular Carcinoma, Glioblastoma Multiforme, Colorectal Cancer, Lung Cancer, Breast Cancer, Prostate Cancer, Pancreas Cancer, Bladder Cancer, and Ovarian Cancer.
- Adenoviridae, Herpesviridae, Rhabdoviridae, Parvoviridae, Picornaviridae, Rooviridae, Poxviridae are the viruses being tested
- These viruses replicate selectively in cancer cells and then lyse cancer cells

2. Correct Genetic Disorders:

Adeno-associated viruses (AAVs) Example: AAV8 vector expressing Factor IX for treatment of Hemophilia B decreasing bleeding episodes by 90%

3. Fight Pathogenic Viral Infections

4. Used in Genetic Studies to Determine Molecular Mechanisms

Used in insecticides

Used to increase drought tolerance in some plants