

1 Zoonosis

Word Origin - Greek

1. Zoon - Animals
2. Noson - Disease

2 What Are Zoonoses?

Infectious diseases that are transmissible from vertebrate animals to humans under natural conditions (WHO)

Zoonotic Spillover: The event in which a pathogen jumps from animal to human (or vice versa)

Zoonoses represent a major public health problem worldwide

1. 60% of known infectious diseases in people are spread from animals
2. Significant morbidity and mortality
3. Impacts regional / global economies

2.1 Is Dengue a Zoonosis?

Infected person → infected mosquito (*Aedes aegypti*) → healthy person

→ Began as a zoonosis (from monkeys) but is now endemic to humans

3 Characteristics of Zoonotic Pathogens

1. Can be stably established in animal populations
2. Can transmit from animals to people with little or no subsequent person-to-person transmission
Ex: West Nile virus / Rabies virus
3. Can spread efficiently between people once introduced from an animal reservoir
Leading to epidemic (Ebola virus)
Or pandemic (Pandemic influenza / Coronaviruses)

4 Transmission routes

1. Fecal Oral (Hantavirus)
2. Inhalation (Coronaviruses)
3. Contact with body fluids (Nipah virus)
4. Penetrating wounds (Rabies virus)

5. Vector transmitted — Mosquitoes and ticks (West Nile virus)

Zoonotic because birds are host reservoir

4.1 Reverse Zoonoses

As of September 2022, the human SARS-CoV-2 virus has been detected in 25 animal species

5 Nipah Virus

Endemic to fruit bats in Southeast Asia

→ Virus doesn't affect bats, but they are carriers and can spread it through bodily fluids (saliva or urine)

5.1 Malaysia - 1998-1999

1. Transmission facilitated by intermediate hosts
2. Infection of pigs

Pig-to-pig → pig-to-human by aerosol

6 Disease

Most cases are symptomatic

Fatality of 40-100%

Causes severe, rapidly progressive encephalitis

→ May have delayed onset or relapse, months or years after infection

Can cause respiratory involvement or respiratory illness

→ May cause acute respiratory distress syndrome

Can spread through:

1. Consumption of contaminated food or fruit products such as raw date palm juice
2. Close contact with an infected person's bodily fluids

6.1 Bangladesh

Nearly annual outbreaks in Bangladesh

Solved with rudimentary nets above date palm trees



Figure 1: Date palm nets

7 Factors That Influence Spillover Events

7.1 Reservoir Host Distribution

Affected by interactions between species:

1. Geographic range overlap
2. Travel
3. Hunting, trade, and consumption of meat from wild species

7.2 Reservoir Host Density

Ex: Hantaviruses transmitted through deer mice (10-12% carriers) in Yosemite deluxe cabins

→ Deer mice burrowing in styrofoam insulation

Cause diseases such as:

1. Hantavirus pulmonary syndrome (HPS)
2. Hemorrhagic fever with renal syndrome (HFRS)

7.3 Animal Host-Associated Factors

Bats are often reservoirs because their immune system can deal with a wide variety of pathogens

→ Tuned down immune response because of flight adaptations

Ecological habits of animals which frequently share the environment with humans and domestic / livestock animals

Some animals can act as intermediate hosts in spillover events

7.4 Human Host-Associated Factors

1. Immunological Factors

2. Genetic Factors
3. Behavioral Factors

7.5 Phylogenetic Distance Between Host Species

Risk of spillover is higher among species with greater phylogenetic proximity

Phylogenetically distant hosts may cause more virulence

7.6 Characteristics of the Pathogens

‘Generalist’ pathogens (as opposed to ‘specialist’) have the ability to infect a broad host range and are more able to jump the barrier between species

Different viral taxonomic groups have varied zoonotic potential

Viruses and their hosts are in a constant arms race

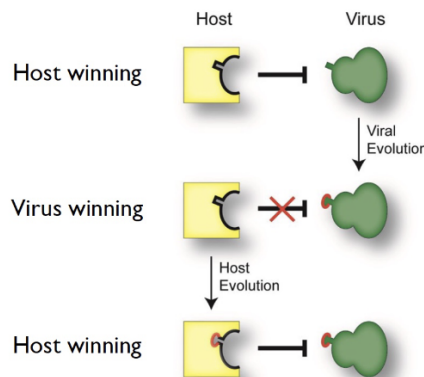


Figure 2: Viruses and hosts evolve to survive

7.7 Environmental Factors

1. Loss of biodiversity is associated with emergence and spread of infectious disease
2. Change in land use
3. Global warming modifies the behavior of reservoir species and recipient hosts

8 The One Health Challenge

The health of people is closely connected to the health of animals and our shared environment

→ Health issues need to be fought at the human-animal-environment interface

9 Bats

Many different viral families are found in bats, but most don't appear to make them sick

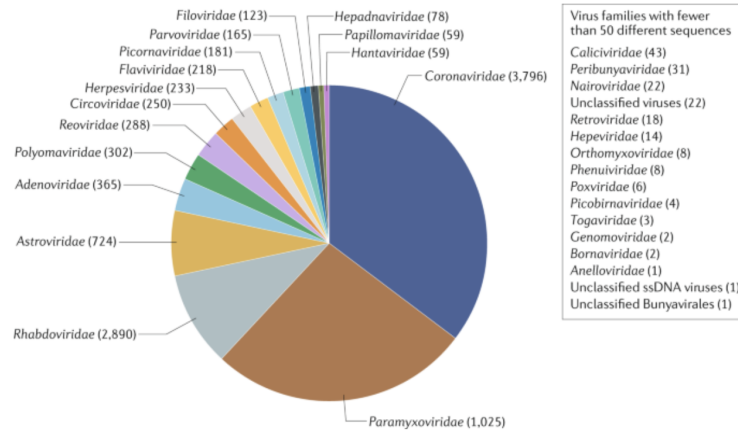


Figure 3: Viruses found in bats

9.1 SARS-CoV-2

Seventh coronavirus known to infect humans

→ Generally begins in bats and goes through an intermediate host

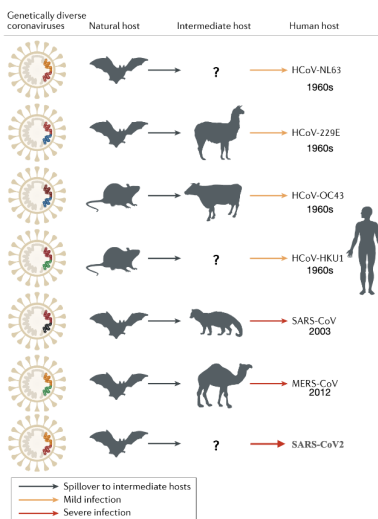


Figure 4: Coronaviruses in humans

9.2 Why are Bats Special?

1. Second most diverse mammalian order on Earth after rodents and are gregarious (living in social colonies)
 - Facilitates rapid transmission of pathogens
 - Large populations could sustain acute-immunizing infections
 - Selects for viruses that can adapt to novel host environments
2. Frequent interaction with humans
 - Peridomestic habits
 - Bushmeat
 - Deforestation
3. Relatively long lifespan (3-10x longer than equivalently-sized mammals)
 - Facilitate viral persistence for chronic infections
4. Fly long distances
 - Allows dispersal over long distances
 - Flight may mimic fever
5. The classical pathology caused by strong activation of the immune system in response to viral infection that is seen in humans (cytokine storm) does not occur in bats
 - Weakened DNA sensing
 - Due to the high metabolic requirement of flight
 - Some aspects of innate immune system are always 'on'

10 Animal-Human Transmission

Most animal viruses are unable to replicate in the human body

→ Of those that can, fewer are transmissible between humans or human-exclusive

10.1 Obstacles to Replication in New Hosts

1. Needs to interact with many different cellular proteins in order to enter a new cell and replicate
2. Needs to evade immune responses of the host

10.1.1 Viral Life Cycle

1. Attachment
2. Penetration

3. Uncoating
4. Replication
5. Assembly
6. Release

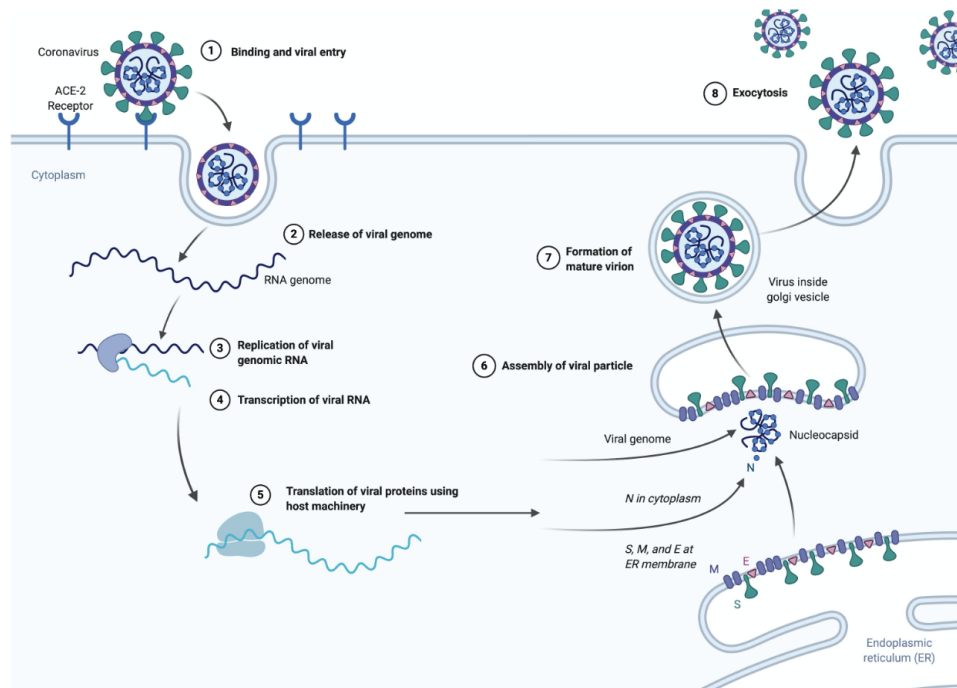


Figure 5: Viral life cycle

Viruses exploit host cell machinery for all aspects of their multiplication

→ Animal viruses will only replicate in humans if they can interact with all the useful proteins that they need

10.2 Viral Sensing

Cells monitor their intra and extracellular spaces for the presence of atypical nucleic acid (wrong location or unusual structure) associated with viral infection

1. Cytosolic DNA
2. Double-stranded RNA
3. Unusually capped mRNA

10.2.1 Interferon Pathway

When a cell is infected, viral PAMPS are recognized by specific receptors

→ Initiates events, ultimately resulting in the infected cells releasing a small set of molecules called interferons (IFN)

→ Cells which detect IFN will start making proteins whose function is to combat viral infection

To replicate within a host, viruses need to inhibit the IFN response

→ Hiding dsRNA (replicating genome) is one strategy used to prevent being detected and eliminated

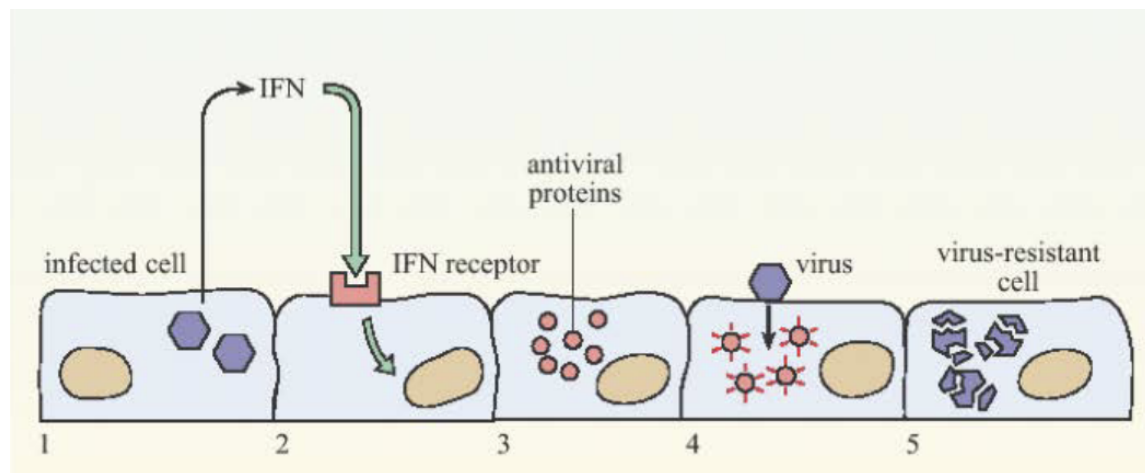


Figure 6: IFN Pathway

Ex: OAS / RNase L pathway was one of the first ISG (interferon stimulated gene) antiviral mechanisms to be identified

→ RNase indiscriminantly destroys RNA

10.2.2 Infecting New Hosts

Often, pathogens must adapt to successfully infect a novel host

1. Use different cell surface receptors
2. Escape a novel type of immune response
3. Ensure they are transmitted by the new host

RNA viruses are the most likely to be associated with spillover events because of their

1. High mutation rates

2. High multiplication rates