

**Crossing the Species Barrier:  
Severe Acute Respiratory Syndrome Coronavirus**  
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## Introduction

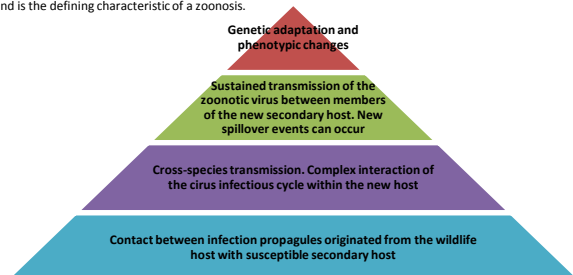
The emergence of new infectious diseases is one of the major threats in the human population and the emergence of new viruses by zoonotic processes is within these threats. Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) is the perfect example to explain how viruses can cross the species barrier from animals to human and produce an epidemic.

## Objectives

- ✓ Get to know the phenomenon of Spillover
- ✓ Give a brief description of the Coronavirus family and SARS-CoV
- ✓ Relate the phenomenon of spillover with SARS-CoV
- ✓ Current situation

## Spillover Phenomenon

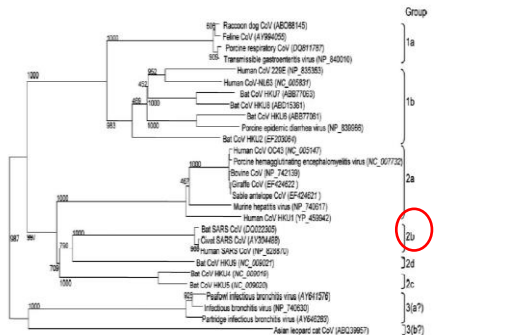
Spillover is the ability of a virus to complete the virus infection cycle in a new secondary host population and is the defining characteristic of a zoonosis.



**Figure 1.** Four transition stages that explain the process of zoonotic disease emergence including zoonotic virus emergence. The process begins at the base of the pyramid. The first two transitions (blue and purple) are prerequisite and the other two stages (green and red) are needed for Pandemic Emergence.

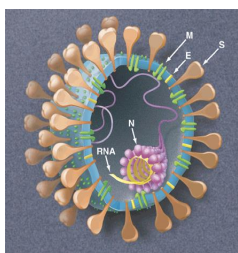
## Coronavirus family

The *Coronaviridae* family, within the order *Nidovirales*, is formed by 36 coronavirus. Members of this family are known to cause respiratory or intestinal infections in humans and other mammalian and avian species.



**Figure2.** Coronaviruses Taxonomy. In this figure we can observe the diversity of avian and mammalian species that coronaviruses can infect. SARS-CoV is a member of the 2b group (red circle). (1)

## SARS-CoV morphology and genome organization



**Figure3.** Structure of SARS-CoV viruses. N: nucleocapsid; M: membrane, E: envelope and S: Spike glycoprotein. <http://www.sciencemag.org/content/300/5624/1377/F1.expansion>

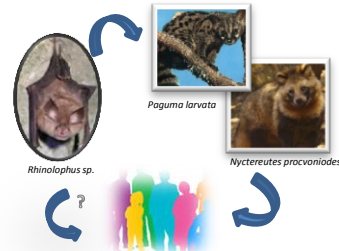
- Single-stranded, positive-sense RNA genome around 30 kb of length. Organized in 13-15 open reading frames (ORFs).
- Non structural genes are replicase and proteases (orf1ab).
- Structural genes are Spike (S), envelope (E), membrane (M), and nucleocapsid (N).
- Spike glycoprotein is involved in the recognition and binding to the host cells receptors. Divided into two domains S1 and S2.



**Figure 4.** Genome organization. Blue box: proteases. Brown box: polymerase/replicase. Green box: Spike protein gen. Red box: Envelope genes. Yellow box: Membrane genes. Orange box: Nucleocapsid genes.

## Contact between species and transmission of the virus

- Serological findings, PCR and genome sequence analysis confirmed the presence of SARS-like coronaviruses in bats of the genus *Rhinolophus*, suggesting that horseshoe bats are the natural reservoir.
- Palm civets and raccoon dogs, that were in contact with horseshoe bats, in wet markets probably, got infected with SARS-CoV. They are the amplifying secondary hosts because no serological findings were achieved in wild animals and they transmitted the virus into the human population.
- Is still not know if it was possible a direct transmission between bats and humans.
- Transmission between humans was due to droplets and fecal-oral transmission.



**Figure 5.** Schematic representation of how SARS-CoV was transmitted into the human population.

### Intrinsic and extrinsic biotic factors and molecular changes in the genome

- ✓ **High replication rates** → RNA-dependent polymerase with a mutation rate of  $10^{-6}$  per nucleotide and per cycle.
- ✓ **High mutation rates:**
  - Hot spots: non-structural protein 3 (nsp3), a cleavage product from the ORF1a polyprotein, Spike protein, ORF3 and ORF8.
- Region Binding Domain (RBD) of the Spike Protein. Key region which influence host range expansion. The residues 479 and 487 are the ones that changed in palm civets and increased the binding affinity for human ACE2 receptor (Figure6)
- ✓ **Homologous recombination** → mammalian ancestry in 5' of the genome (replicase/transcriptase) and avian ancestry in 3' of the genome (where Spike protein is encoded).
- ✓ **Persistence:**
  - Scanning for homologous receptors → gradual accumulation of mutations that alter the Spike affinity for orthologous receptors in different species.
  - Receptor/coreceptor shift: gene acquisition → recognition of completely different receptors
- ✓ **Anthropogenic influences**

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**Figure6:** Changes in the Spike RBD region between different strains of human SARS-CoV, SARS-like coronavirus of bats (BSCoVRP3), SARS-CoV of palm civets (HC/SZ/61/03 and SZ16) and raccoon dogs (A031). (2)

## Current Situation

- A novel coronavirus appeared in Saudi Arabia in September 2012 → Middle East Coronavirus (MERS-CoV). This new virus is not very transmissible between humans but there is a real danger if it spreads to other parts of the world. Member of the 2b coronavirus like SARS-CoV. Bats origin?
- No antiviral or immunomodulator is efficacious or approved for clinical use against coronaviruses
- Intensive care with mechanical ventilation and extracorporeal membrane oxygenation support → the main modalities of treatment.
- No commercial vaccine is available. Different groups of research are working on it targeting mainly the Spike Protein.
- A rapid response, a united global front and mobilization of resources and expertise are our best tools in preventing or reducing the devastation that some of these viruses can cause.

## Conclusions

- SARS-CoV, responsible of SARS disease is a member of the coronavirus family closely related with coronaviruses found in bats and is classified within the group 2b of coronaviruses.
- Palm civets and racoon dogs were only amplifying host that transmitted SARS-CoV into the human population. Bats of the genus *Rhinolophus* are now believed to be the natural reservoir.
- High mutation rates, high multiplication rates, homologous recombination, and persistence are the main characteristics that favoured the migration of SARS-CoV from animals to humans.
- Amino acid changes in the RBD of the Spike protein changed the receptor binding affinity and drive the host range expansion.
- Anthropogenic activities influence the emergence of new viruses. A rapid response, a united global front and mobilization of resources and expertise are our best tools in preventing or reducing the devastation that some of these viruses can cause. This is exemplified by the recent events that have led to the recognition for acute respiratory illness as SARS-CoV and the recent described MERS-CoV.
- Continued surveillance in mammals, bats and birds, which are believed to be the main source of new coronaviruses, will allow better understanding of the ecology of coronaviruses and may aid in the prevention of animal-to-human transmissions and outbreaks of the future.

## References

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