Why is HIV hard to treat?
Viral disguise

Virus mutates and the proteins on its outer surface change.
These new surface proteins are not recognized by the immune system's memory cells.
Mutant virus particles bearing new surface proteins survive immune system attack and begin new round of infection

Each round of infection reduces numbers of helper T cells because they are infected by virus and destroyed.

Furthermore, because each lineage of T cells has a limited capacity for replication, after a finite number of rounds of replication the body's supply of helper T cells becomes exhausted. The immune system eventually is overwhelmed and collapses.

Several different types of drugs have been developed to treat HIV.

- Reverse transcriptase inhibitors (ex. AZT).
- Protease inhibitors (prevent HIV from producing final viral proteins from precursor proteins).
- Fusion inhibitors prevent HIV entering cells.
- Integrase inhibitors prevent HIV from inserting HIV DNA into host's genome.

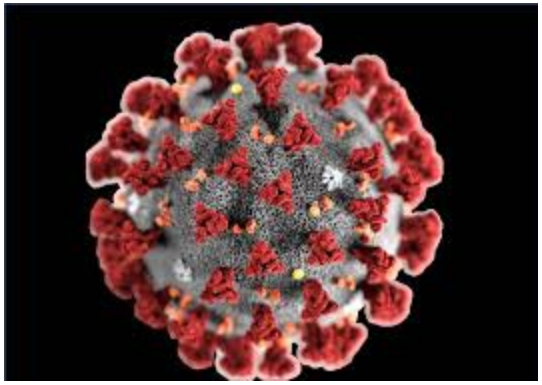
Most successful approach has been to use multi-drug cocktails (referred to as HAART [Highly Active Anti-Retroviral Treatments]

HAART cocktails usually use three different drugs in combination (ex. two reverse transcriptase inhibitors and a protease inhibitor).

Multi-drug treatments have proven very successful in reducing viral load and reducing mortality of patients.

CORONAVIRUS

RETROVIRUS



Coronaviruses cause acute, mild upper respiratory infection (common cold).

Structure

Spherical or pleomorphic enveloped particles containing single-stranded (positive-sense) RNA associated with a nucleoprotein within a capsid comprised of matrix protein. The envelope bears club-shaped glycoprotein projections.

Classification

Coronaviruses are classified on the basis of the crown or halo-like appearance (alone) of the envelope glycoproteins, and on characteristic features of chemistry and replication. Most human coronaviruses fall into one of two serotypes: OC43-like and 229E-like.

Multiplication

The virus enters the host cell, and the uncoated genome is transcribed and translated. The mRNAs form a unique “nested set” sharing a common 3′ end. New virions form by budding from host cell membranes.

Pathogenesis

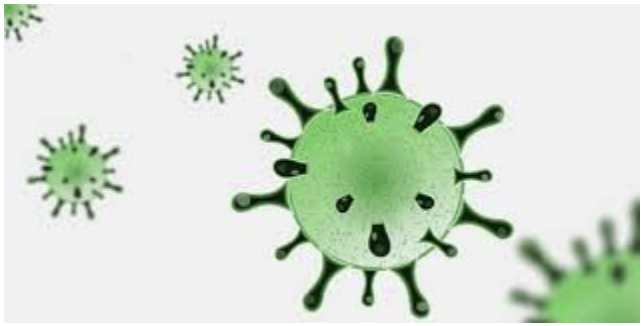
Transmission is usually via airborne droplets to the nasal mucosa. Virus replicates locally in cells of the ciliated epithelium, causing cell damage and inflammation.

Host Defenses

The appearance of antibody in serum and nasal secretions is followed by resolution of the infection. Immunity wanes within a year or two.

Epidemiology

Incidence peaks in the winter, taking the form of local epidemics lasting a few weeks or months. The same serotype may return to an area after several years.



The **coronavirus disease** 2019 (COVID-19) is a new type of pneumonia caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. COVID-19 is affecting millions of patients, and the infected number keeps increasing.

According to World Health Organization (WHO) statistics on March 2020, the mortality rate among confirmed COVID-19 cases was 3.4%. As of May 2020, according to WHO, the mortality rate is nearly 5.9%.

In Italy, however, the mortality rate is more than 13%.

The SARS-CoV-2 coronavirus is a type of single-stranded RNA virus that belongs to the coronaviruses family.

Coronaviruses can be divided into four genera: *Alphacoronavirus* (αCoV), *Betacoronavirus* (βCoV), *Gamma coronavirus* (γCoV), and *Deltacoronavirus* (δCoV).

Currently, seven coronaviruses are known to infect human, including two alphacoronaviruses and five betacoronaviruses .

During the past two decades, three previously unknown betacoronaviruses (SARS-CoV, MERS-CoV, and SARS-CoV-2) have emerged.

These deadly coronaviruses cause lower respiratory tract infections, resulting in acute pneumonia, respiratory distress, cytokine storms, multiple organ dysfunctions, and even patient death.

Tempesta di citochine: molecole che richiamano il sangue → formazione di liquido nei polmoni

Clinical Treatment of COVID-19

Currently there is no specific drug available to block SARS-CoV-2 infection or to kill the viruses. The treatment strategy is mainly determined by the clinical characteristics and severity of the disease, and different patients receive different treatments based on their conditions.

Generally, patients are treated with strengthening support therapy to maintain sufficient caloric intake and water and electrolyte balance. Strategies including oxygen therapy, antiviral therapy, immunotherapy, organ support, and complication prevention are used for the prevention and control of acute respiratory distress syndrome, cytokine storms, organ failure, and secondary hospital infections.

https://www.youtube.com/watch?v=i0ZabxXmH4Y

The known transmission pathways of SARS-CoV-2 in humans include the following:

(1)inhaling tiny droplets carrying virus,

(2) close contact with virus carriers,

(3) contact with a surface contaminated by SARS-CoV-2,

(4) aerosol transmission.

After the membrane fusion, the viral RNA genome is released into the cytoplasm of the host cells.

After RNA replication, the structural proteins N, S, E, and M are translated S, E, and M proteins insert into the endoplasmic reticulum (ER) and move to the endoplasmic reticulum-Golgi intermediate compartment to form the mature viruses with the viral genome and N protein.

After that, viruses are transported to the cell surface and then released out of the cells by exocytosis