

Understand the Coronavirus

Systematic name of the virus: 2019-nCoV
Popular virus name: COVID coronavirus (*coronavirus*)
The names of the disease: COVID-19, SARS-CoV-2
SARS - short for: *Severe Acute Respiratory Syndrome*
n - short for: *novel*
CoV - short for: *Corona Virus*

Paweł Grieb^{*,#} and Bogdan Lesyng^{**,#}

* prof. dr hab. n. med., Mossakowski Medical Research Centre, Polish Academy Science, Department of Experimental Pharmacology

** prof. dr hab. n. fiz., University of Warsaw, Faculty of Physics, Department of Biophysics IFD, Lab. for Molecular Design and Bioinformatics


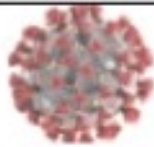



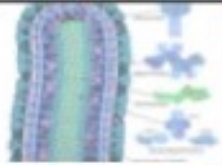




The authors of this presentation present thoughts based on their current knowledge, not on the findings or expertise of the institutions in which they are employed.

The state of the world as at March 14, 2020 at approx. 22:00
(GMT + 1), data from: <https://www.worldometers.info/>

| | |
|--------------------------------|---------------|
| Liczba ludzi : | 7.770.880.000 |
| Od początku roku urodziło się: | 28.355.000 |
| zmarło: | 11.903.000 |
| w tym na gripę: | 98.343 |
| na HIV/AIDS: | 340.220 |
| na malarię: | 198.516 |
| popeniło samobójstwo: | 217.030 |
| zginęło na drogach: | 273.205 |
| ZACHORWAŁO NA COV-19: | 155.839 |
| ZMARŁO NA COV-19: | 5.814 |

Should we be afraid of the 2019-nCoV coronavirus ?

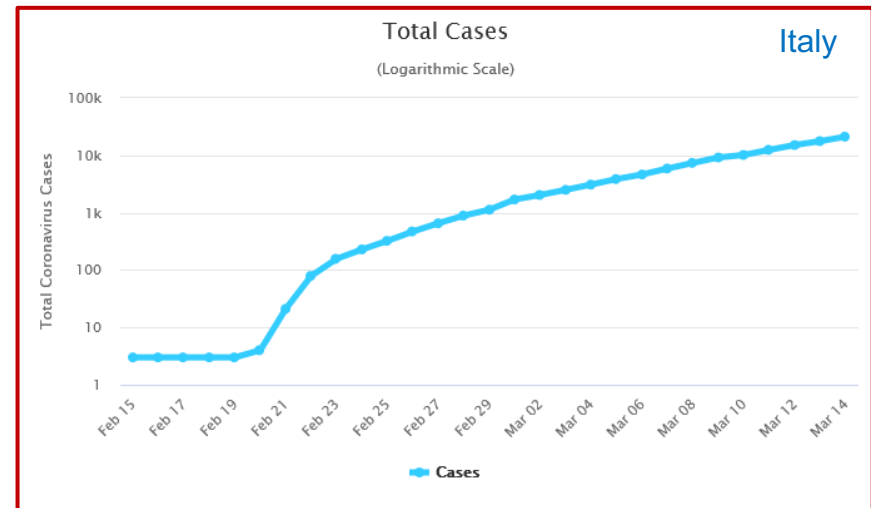
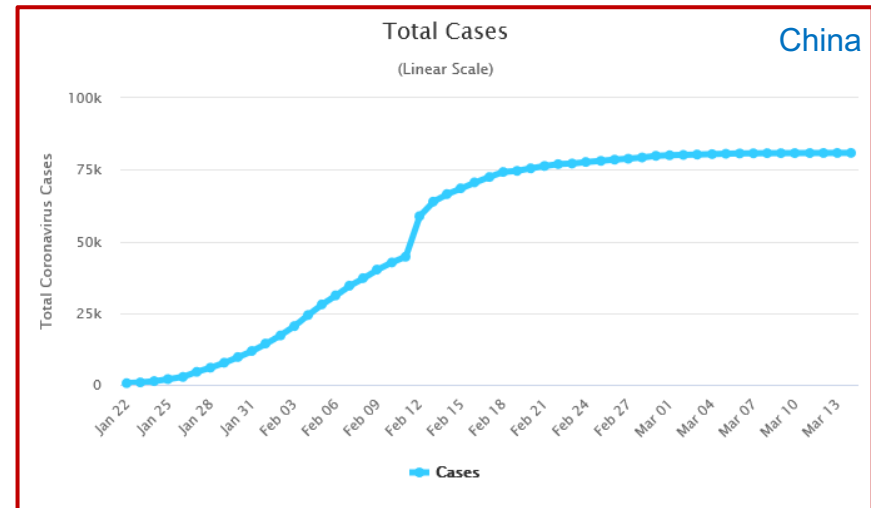
A brief history of the epidemics in the 21st century

| Epidemia | Liczba chorych | Liczba ofiar | Prawdopodobny nosiciel | Struktura wirusa |
|--|-----------------------------|---|--|--|
| | | | | |
| SARS 2002/2003 | 8500 | 774 |  |  |
| MERS 2012/2017 | 2500 | 862 |  |  |
| EBOLA 2014/2019 | 30 000 | 11 000 |  |  |
| ZIKA 2014/2016 | (??) | ok. 3 tysiące urodzonych dzieci z małogłowiem |  |  |
| COVID-19 2019/2020 → (?) WHO stan na 18.03.2020 | 191 127 (74 760) | 7 807 (3 352) |  |  |
| | W nawiasach dane dla Europy | | | |

- Typical carriers of viruses dangerous to humans and other animals are, among others bats or camels that have very efficient immune systems, and therefore different types of germs are less harmful to them.
- To determine whether a virus has spread from an animal to a human, the degree of similarity (homology) of the genome of animal and human viruses is determined. For coronavirus, there was 99% similarity between the genomes of pangolin and human viruses.

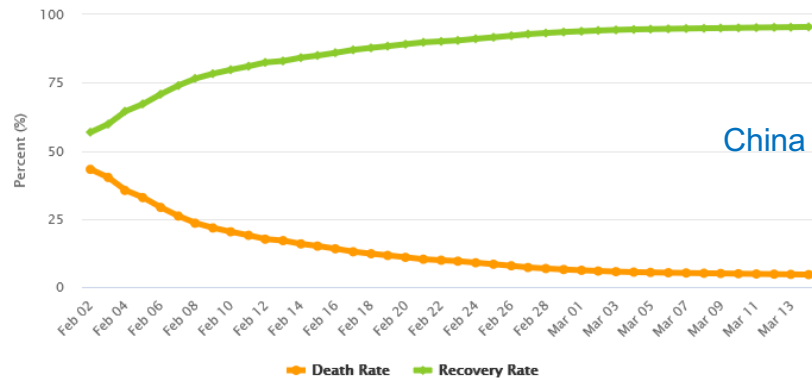
- Unfortunately, we have something to fear because the epidemic turned into the first pandemic of the 21st century. According to WHO pandemic is "the spread of the new disease worldwide."
- The COVID-19 outbreak began at the end of 2019 in Mainland China, in the city of Wuhan, the capital of Hubei Province. Because of the Chinese authorities radical countermeasures (harsher than those currently used in our country) on February 19, 2020, the development of this epidemic in China was basically controlled and it seemed for a moment that a pandemic would not occur. However, at the beginning of March 2020 the number of people infected with COVID-19 coronavirus has increased in Europe, in particular in Italy.
- Currently, the increase in the number of people infected in some areas of the world has become exponential. The source of this increase lies in Europe, but infected people have already been found in 134 countries / territories on all continents. Compare the next diagrams.

Data from: <https://www.worldometers.info/coronavirus/>



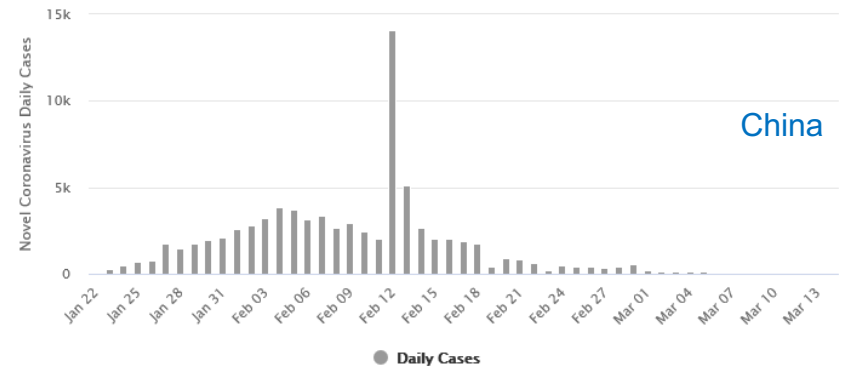
Outcome of total closed cases (recovery rate vs death rate)

(Cumulative total deaths and recoveries over cumulative number of closed cases)



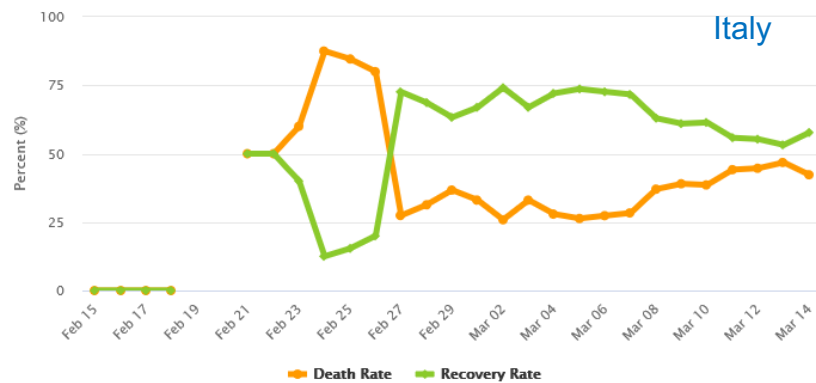
Daily New Cases

Cases per Day
Data as of 0:00 GMT+0



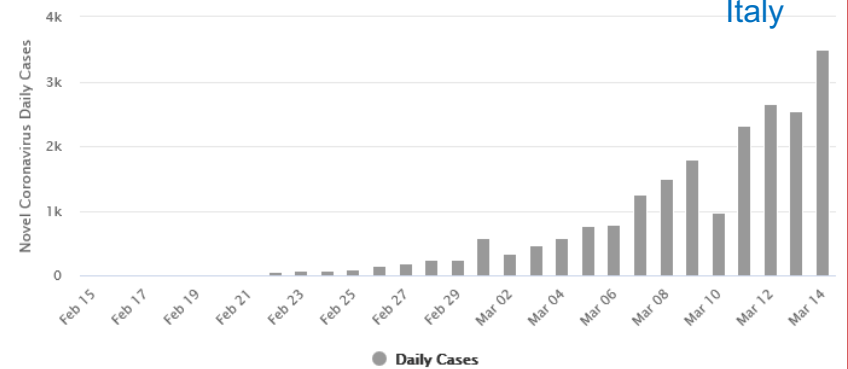
Outcome of total closed cases (recovery rate vs death rate)

(Cumulative total deaths and recoveries over cumulative number of closed cases)

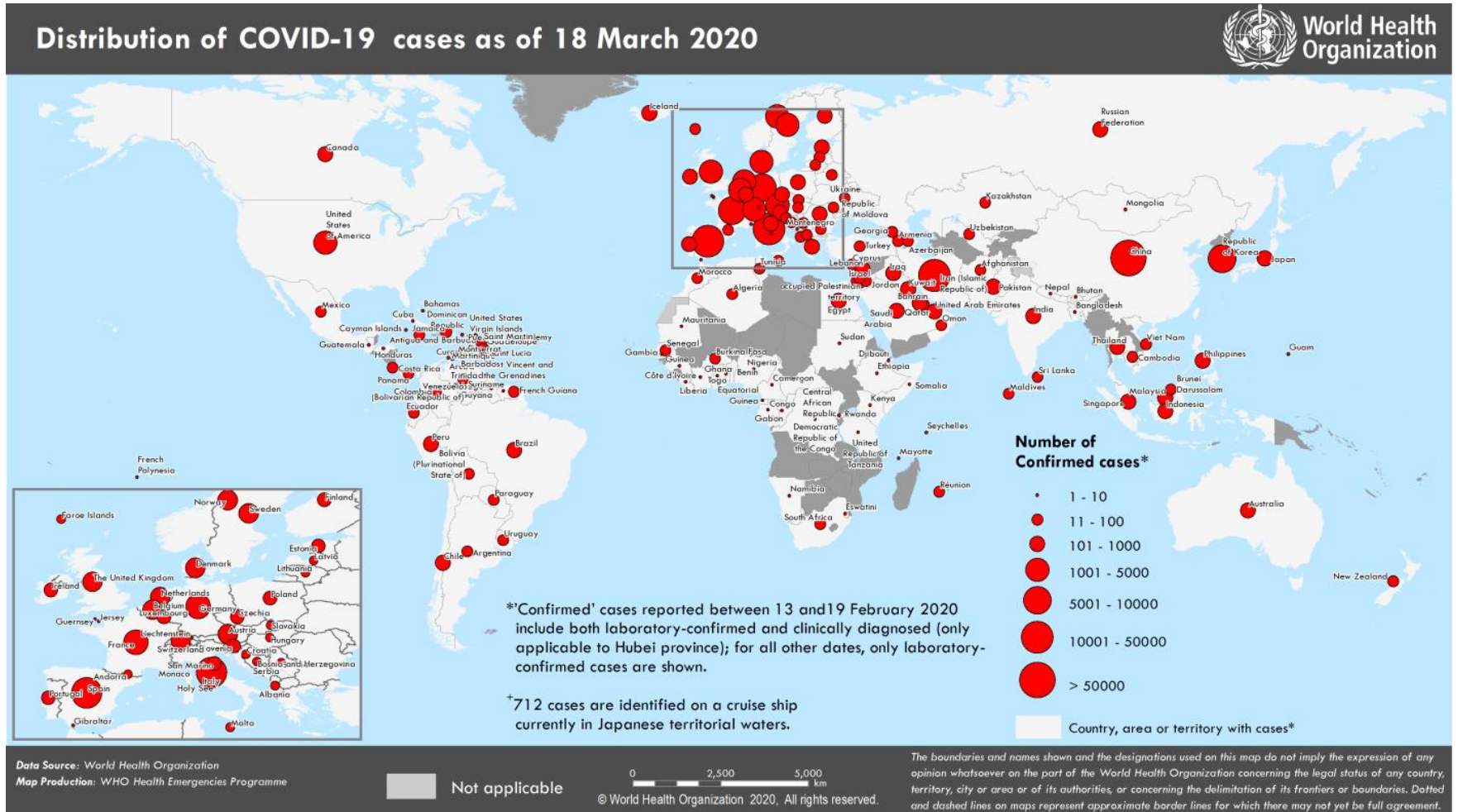


Daily New Cases

Cases per Day
Data as of 0:00 GMT+0



Map of the pandemic, as of March 18, 2020



WHO (World Health Organization) data

https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200318-sitrep-58-covid-19.pdf?sfvrsn=20876712_2/

Tabela 1. Porównanie infekcji koronawirusowych z innymi chorobami wirusowymi.

| Wirus | Ryzyko zgonu | R ₀ | Szczepionka? | Skuteczny lek? |
|----------------|--------------|----------------|--------------|----------------|
| Wścieklizna | 100% | <1 | TAK | Nie |
| HIV | ~ 90% | 3,4 | NIE | TAK |
| Ebola | 74% | 2,3 | NIE | NIE |
| MERS-CoV | ~ 40% | <1 | NIE | NIE |
| Ospa prawdziwa | ~ 30% | 5-7 | TAK... | Nie |
| Odra | 0,3% | 12-18 | TAK | Nie |
| Ptasia grypa | ~ 50% | <1 | NIE... | TAK... |
| AH1N1v – 2009 | 0,03% | 1,2-1,6 | TAK | TAK |
| AH1N1 – 1918 | 3% | 1,4-3,8 | TAK | TAK |
| Rhinovirus | <0,01 | 6 | NIE | NIE |
| COVID-19 | 1-3% | 1,4-5,5% | NIE | NIE |

Replication rate ("basic reproduction number", R₀) - average number of people who will be infected by 1 infected person:

- R₀ < 1 → the disease will disappear on its own;
- R₀ = 1 → the disease will be stable;
- R₀ > 1 → epidemic risk.

(Rhinovirus - the virus that accounts for 80% of colds)

Regional Medical Chamber in Gdańsk (2020).

Information material on COVID-19, available to doctors as part of an online subscription

Tabela 2. Śmiertelność u chorych objawowych z COVID-19

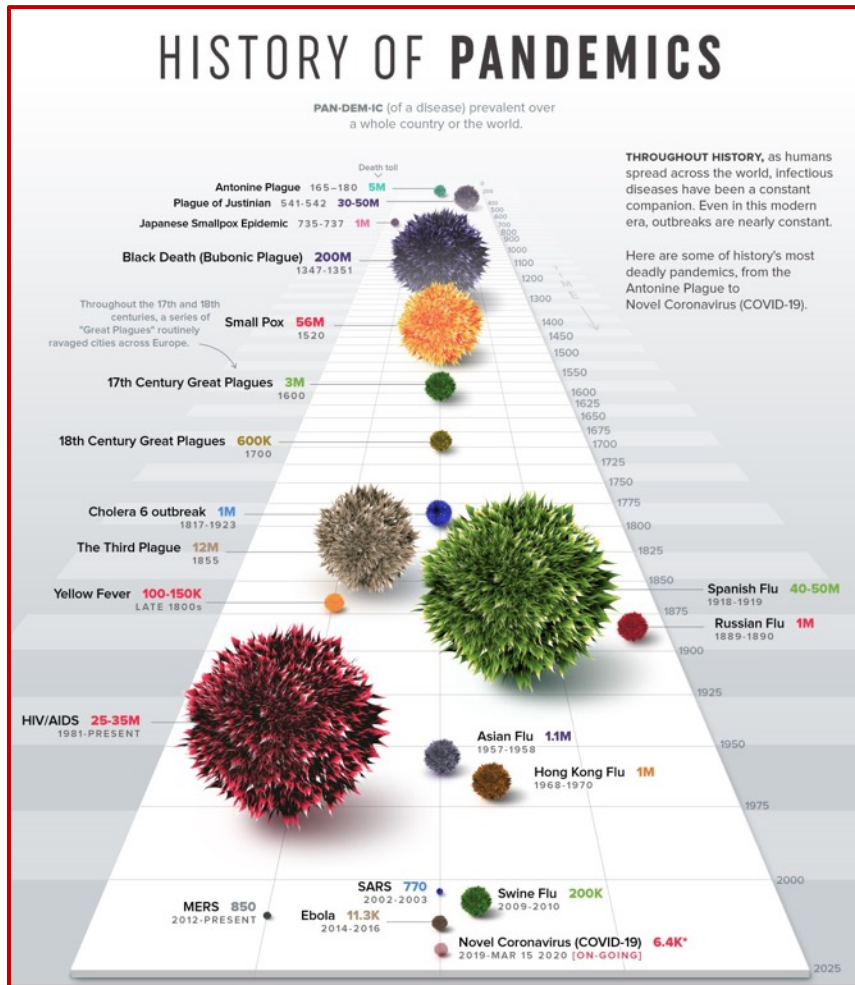
| WIEK w latach | ŚMIERTELNOŚĆ przypadki potwierdzone | ŚMIERTELNOŚĆ wszystkie przypadki |
|---------------|--|-------------------------------------|
| 80+ | 21,9% | 14,8% |
| 70-79 | | 8,0% |
| 60-69 | | 3,6% |
| 50-59 | | 1,3% |
| 40-49 | | 0,4% |
| 30-39 | | 0,2% |
| 20-29 | | 0,2% |
| 10-19 | | 0,2% |
| 0-10 | | 0% |

Tabela 4. Wpływ chorób towarzyszących na śmiertelność w COVID-19.

| CHOROBY TOWARZYSZĄCE | ŚMIERTELNOŚĆ przypadki potwierdzone | ŚMIERTELNOŚĆ wszystkie przypadki |
|---------------------------|--|-------------------------------------|
| SERCOWO-NACZYNIOWE | 13,2% | 10,5% |
| CUKRZYCA | 9,2% | 7,3% |
| PRZEWLEKŁA CHOROBA PŁUC | 8,0% | 6,3% |
| NADCIŚNIENIE TĘTNICZE | 8,4% | 6,0% |
| CHOROBA NOWOTWOROWA | 7,6% | 5,6% |
| BEZ CHORÓB TOWARZYSZĄCYCH | | 0,9% |

Regional Medical Chamber in Gdańsk (2020).
Information material on COVID-19, available to doctors as part of an online subscription.

COVID-19 pandemic compared to other pandemics



The COVID-19 pandemic is neither the first, nor probably the last. Today, it is definitely not the biggest pandemic in the history of human civilization. However, it develops quite rapidly.

Looking at the picture next to it, we should pay attention not only to the size of a given pandemic, but also to its dynamics as a measure of its potential for further development. Unfortunately, the ball representing the COVID-19 pandemic is "hot" and the fight against it is just beginning.

We will manage, but it is certain that we will suffer significant losses. To minimize them, we must first get to know the enemy well.

<https://www.visualcapitalist.com/history-of-pandemics-deadliest/>

Some more important scientific papers and information services summarizing the current state of knowledge about the COVID-19 coronavirus

Publication in Nature: “*Why does the coronavirus spread so easily?*”:

- <https://www.nature.com/articles/d41586-020-00660-x/>

Publication in Lancet: “*Genomic characterisation and epidemiology of 2019 novel coronavirus*”:

- [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30251-8/fulltext/](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30251-8/fulltext/)

Publication in *Ann. Rev. Virol.*: “*Structure, function and evolution...*”:

- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5457962/>

Service “Worldometer”

- <https://www.worldometers.info/>

Service: “Hello Zdrowie” z wykorzystaniem opinii specjalistów PAN:

- <https://www.hellozdrowie.pl/koronawirus-polska-akademia-nauk-opublikowala-informator-o-koronawirusie/>

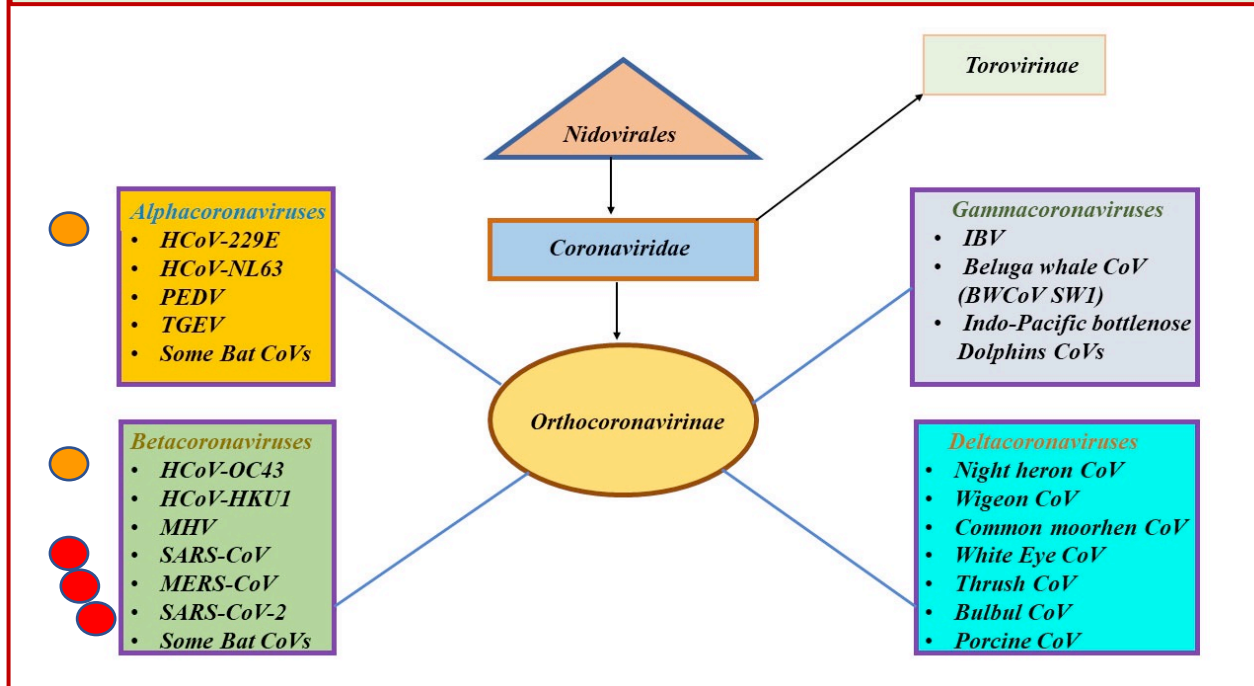
Service: Massachusetts *Peace Action*:

- <http://masspeaceaction.org/coronavirus-structure-vaccine-and-therapy-development/>

Service: Swiss Institute of Bioinformatics:

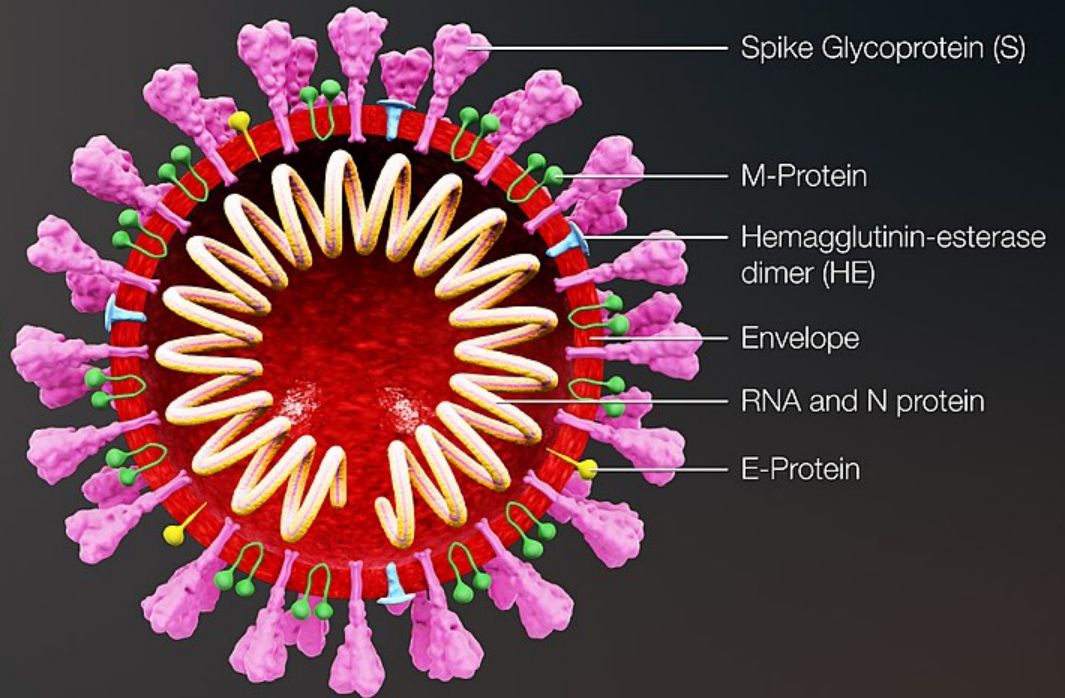
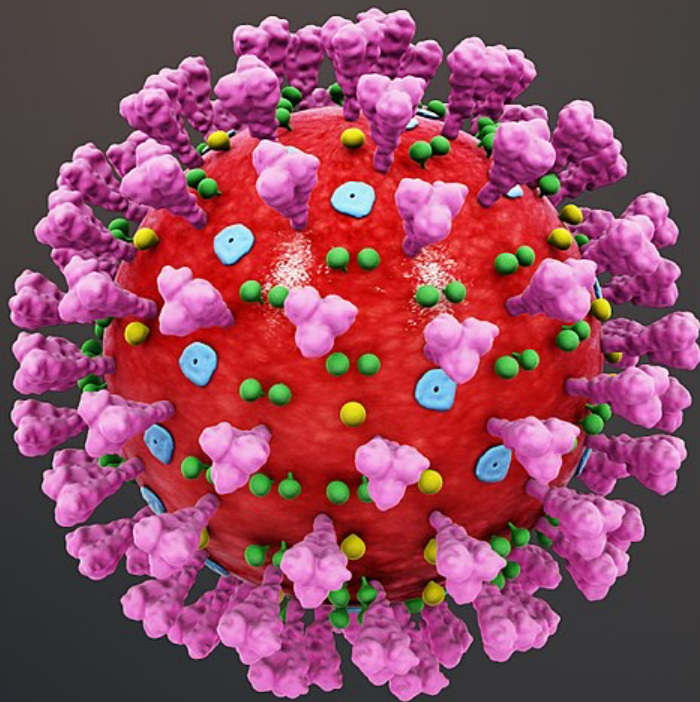
- https://viralzone.expasy.org/30?outline=all_by_species/

Many coronaviruses have been discovered - most only attack animals, however



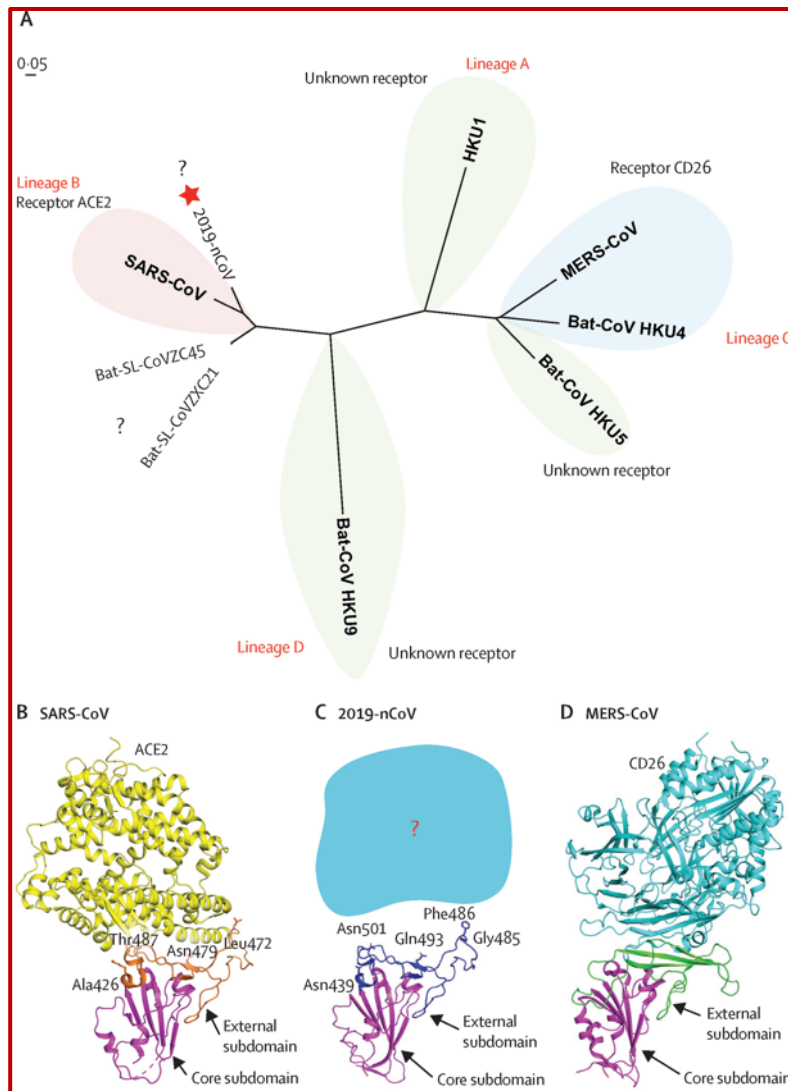
... two cause **common colds and runny nose**, and three others – **very serious diseases (SARS, MERS i COVID-19)**

[Ashour i wsp., *Pathogens* 2020;9:186]



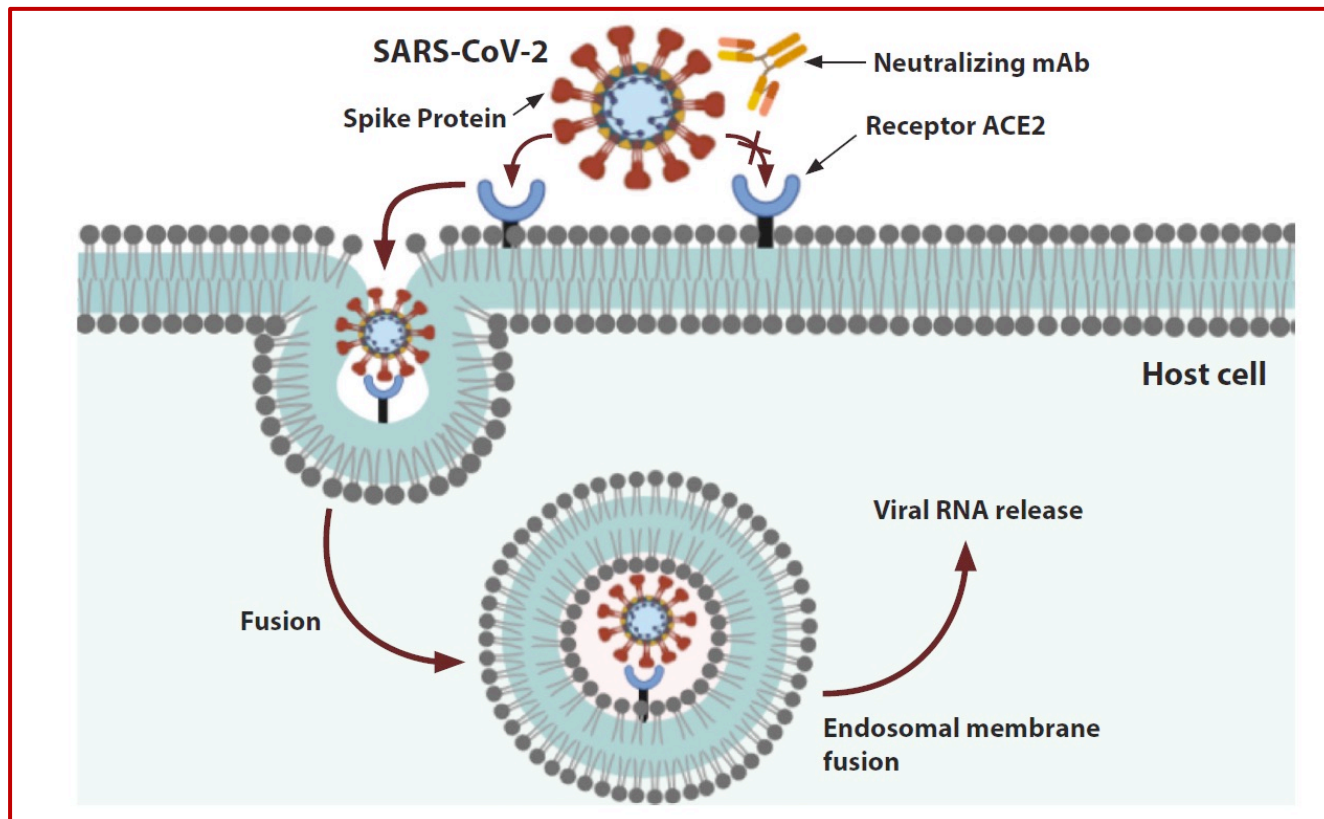
Coronavirus structure. Data from the "commons.m.wikimedia"

website [https://commons.m.wikimedia.org/wiki/File:3D_medical_animation_coronavirus_structure.j](https://commons.m.wikimedia.org/wiki/File:3D_medical_animation_coronavirus_structure.jpg)



Relatively much is already known about the amino acid sequence and 3D structure of a number of key proteins of the 2019-nCoV virus, in particular comparing them with the analogous objects of older pathogenic viruses: SARS-CoV and MERS-CoV, as well as comparing the sequences with all other coronaviruses.

Comparative phylogenetic analysis of known coronaviruses as well as comparative structural analysis of the viral, 2019-nCoV, SARS-CoV and MERS-CoV domains that bind to cell receptors. see R. Lu et al. *Lancet*, 395, 565-574, 2020, [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(20\)30251-8/fulltext/](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30251-8/fulltext/)

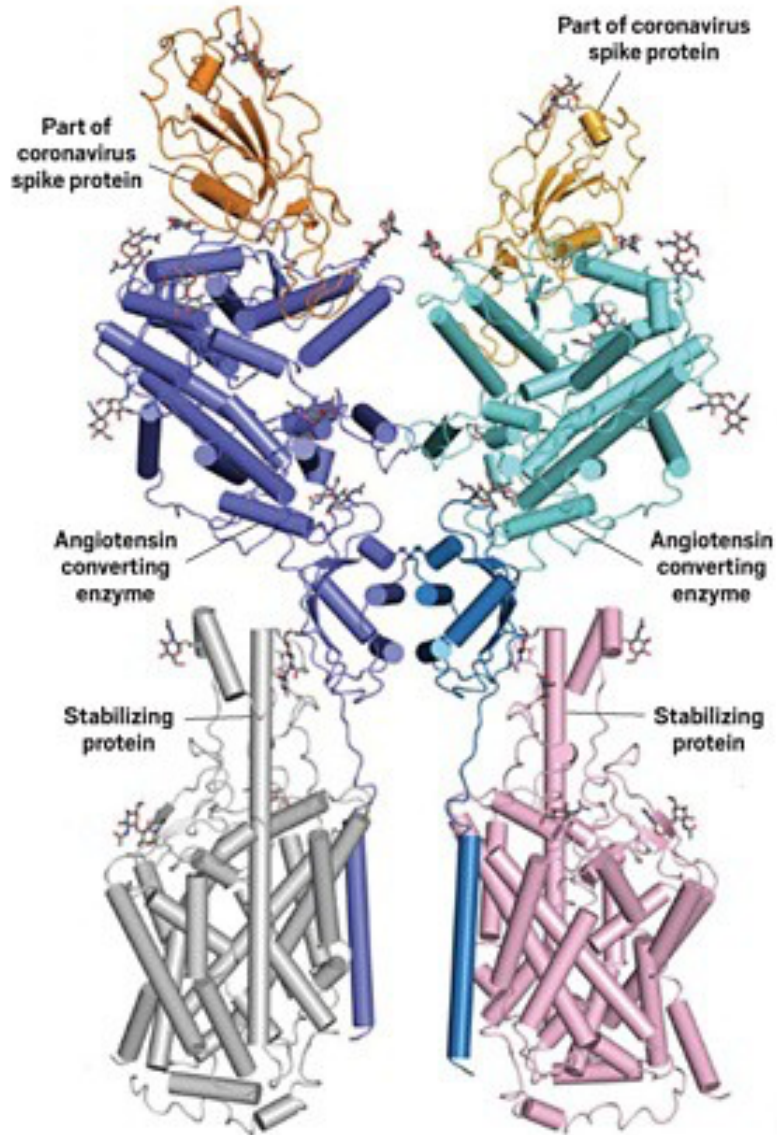


Simplified pattern of COVID-19 coronavirus activity.

It enters the cells, connecting to the ACE2 receptor, which is on the surface of the alveoli, but also on many other cells in the body. The correct defense response is when the cells of the immune system produce antibodies to neutralize the virus. This requires a functioning immune system and lasts at least several days.

Shanmugaraj i wsp.,
Asian Pac. J. Allergy. Immunol 2020 (Epub)

Outside the cell



Inside the cell



Understanding the mechanisms of infection by 2019-nCoV goes to a more detailed molecular level. The structure on the left presents the first step of the infection process. Cylinders mean so-called α -helical protein fragments. The structure was determined by a Chinese team using the cryo-EN technique, see Science, 2020. DOI: 10.1126 / science.abb2762.

The structure at the top presents the main viral protease, the enzyme - a molecular machine involved in the production of some "prefabricated" components of the final virus structure. The computer presentation is different from the one on the left. Helical fragments are cylinders in a more detailed representation, and flat fragments with arrows are so-called structures β . Data comes from Protein Data Bank,

<http://www.rcsb.org/news?year=2020&article=5e3c4bcba5007a04a313edcc/>

What to do not to be powerless?

Here are some directions of action:

I. Epidemiological activities:

- a. limiting the scope of a pandemic - mass detection of infected people, tracking infection chains, quarantine of infected people,
- b. delaying the pandemic development - limitations in everyday life, social isolation,
- c. understanding the mechanisms (what animals are the reservoir, what is the mechanism of the disease, etc.).

II. Pharmacological actions:

- a. antiviral drugs (synthetic, from natural sources ...),
- b. supportive medication (many proposals ...),
- c. biological drugs (e.g., immunoglobulins from the blood of healers, monoclonal antibodies),
- d. vaccines.

III. Diagnostic and forecasting activities:

- a. rapid and mass detection of genetic material of the virus in humans,
- b. tests to predict the dangerous development of infection and qualify patients for appropriate therapies.

Very brief description of coronavirus identification tests - below are elements of a typical test:

- Genetic material (RNA) is isolated from oral swabs,
- RNA is transcribed into DNA using reverse transcriptase systems,
- The number of DNA molecules is multiplied by means of PCR (*Polymerase Chain Reaction*) technology,
- In the DNA sample, the presence of three genes is identified: E-Gene, RdRP-Gene and N-Gene, characteristic of coronavirus genetic information.

The procedure using conventional methods takes about 8 hours or longer. On the other hand, there are already almost fully automated technologies limiting the analysis time to 4 hours and - importantly - allowing the simultaneous analysis of a large number of samples - up to several hundred a day.

Reagent kits for fast (4h) and automated virus detection
are now approved and manufactured

Roche Diagnostics receives emergency approval for new COVID- 19 test

Posted: 9:53 PM, Mar 13, 2020

<https://www.theindychannel.com/coronavirus/roche-diagnostics-receives-emergency-approval-for-new-covid-19-test>

Thermo Fisher to produce millions of coronavirus diagnostic tests

By [Matthew Herper](#)² [@matthewherper](#)³

March 14, 2020

<https://www.statnews.com/2020/03/14/thermo-fisher-to-produce-millions-of-coronavirus-diagnostic-tests>

There is no drug with proven efficacy in COVID-19 disease, so various drugs are tested, especially those which in clinical or preclinical studies have proved effective against infections caused by other viruses, in particular those whose genetic material consists of RNA.

Testing, testing

Promising drugs to treat covid-19

| Drug | Current use | Original mode of action | Being tested? |
|---------------------------------|--------------------------------|---------------------------|-----------------|
| Chloroquine | Antimalarial | Heme polymerase inhibitor | Yes |
| Kaletra (ritonavir + lopinavir) | HIV | Protease inhibitor | Yes |
| Interferon alfa-2b | Hepatitis-C | Immune modulator | Yes |
| Remdesivir | Experimental | Nucleotide analogue | Yes |
| Favipiravir | Influenza | RNA polymerase inhibitor | Yes |
| Actemra (tocilizumab) | Rheumatoid arthritis; covid-19 | Anti-inflammatory | Approved* |
| Kevzara (sarilumab) | Rheumatoid arthritis | Anti-inflammatory | Trials expected |

Source: WHO, adapted from landscape analysis, 17th February 2020

*For use on covid-19 in China, March 2020

Recommended medications, based on the results of clinical studies performed in China, for use in the therapy of patients with COVID-19

58

Drug Discoveries & Therapeutics. 2020; 14(1):58-60.

Communication

DOI: 10.5582/ddt.2020.01012

Discovering drugs to treat coronavirus disease 2019 (COVID-19)

Liying Dong¹, Shasha Hu², Jianjun Gao^{1,*}

¹Department of Pharmacology, School of Pharmacy, Qingdao University, Qingdao, Shandong, China;

Table 1. Antivirals included in the Guidelines (version 6) for treatment of COVID-19

| Drug | Dosage | Method of administration | Duration of treatment |
|-----------------------|---|--------------------------|-----------------------|
| IFN- α | 5 million U or equivalent dose each time, 2 times/day | Vapor inhalation | No more than 10 days |
| Lopinavir/ritonavir | 200 mg/50 mg/capsule, 2 capsules each time, 2 times/day | Oral | No more than 10 days |
| Ribavirin | 500 mg each time, 2 to 3 times/day in combination with IFN- α or lopinavir/ritonavir | Intravenous infusion | No more than 10 days |
| Chloroquine phosphate | 500 mg (300 mg for chloroquine) each time, 2 times/day | Oral | No more than 10 days |
| Arbidol | 200 mg each time, 3 times/day | Oral | No more than 10 days |

China Endorses Avigan / Favipiravir For COVID-19 Disease Treatment

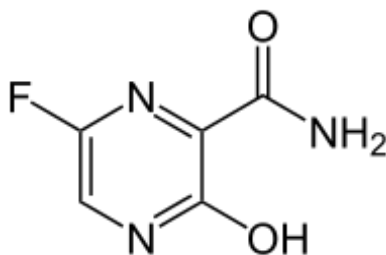
Avigan Favipiravir (T-705) is a broad-spectrum inhibitor of viral RNA polymerase

“Zhang Xinmin, China’s director of the National Center for Biotechnology Development said Avigan (Favipiravir) was found to be effective in 2 clinical trials completed in Wuhan and Shenzhen and involved 240 patients and 80 patients respectively. During a conference in Beijing on March 17, 2020, Zhang said the medicine worked for coronavirus-related symptoms including pneumonia and had no obvious side effects.”

“The director said he formally recommended the use of this medicine as a way to treat the COVID-19 disease, which is caused by the SARS-CoV-2 virus.”...

”According to Zhang, a Chinese pharmaceutical company has been approved by the National Medical Products Administration to mass-produce the medication and ensure a stable supply.”

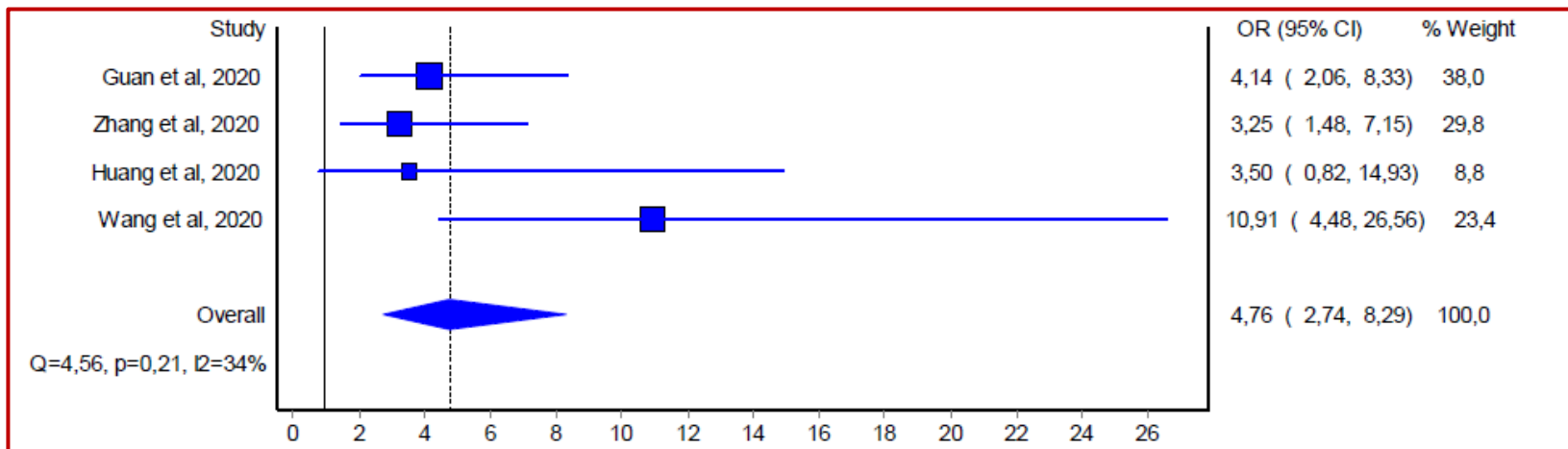
Article: D. W. Hackett, see: <https://www.precisionvaccinations.com/avigan-favipiravir-t-705-broad-spectrum-inhibitor-viral-rna-polymerase/>



This is the first hope

5-Fluoro-2-hydroxypyrazine-3-carboxamide,
Commercial names: T-705, Avigan, Favipiravir

- Understanding the mechanism of the disease will allow the rational use of equipment (e.g. respirators).
- The course of the disease will be hard when a bacterial infection involving the lungs joins the viral infection - and this seems to be predictable.



- Blood levels of procalcitonin protein (pCt) in patients with severe forms of COVID-19 were 4 times higher than normal.
- And pCt *does not* increase in viral infections but *increases* in bacterial ones.



Clinical vaccine studies have already begun

First Patient Dosed in Moderna's COVID-19 Vaccine Trial

Published: Mar 16, 2020 By Mark Terry



<https://www.biospace.com/article/moderna-s-covid-19-vaccine-clinical-trial-starts-today/>

Construction of technology platforms for the creation of RNA-based virus vaccines

The research and implementation works of CureVac from Tübingen (in which Polish researcher Dr. Mariola Fotin-Mleczek oversees the work on the coronavirus vaccine) as well as Moderna Therapeutics from Seattle mentioned in the previous slide deserve special attention.

BioProcess International

One billion doses: CureVac gains \$88m to support capacity for COVID-19 mRNA vaccine

by [Dan Stanton](#) Wednesday, March 18, 2020 10:44 am

CureVac – the German biotech at the center of a Donald Trump acquisition rumor – has received a grant from the European Commission to expedite construction of a plant set to make a potential mRNA vaccine against coronavirus.

The European Commission (EC) offered up to €80 million (\$88 million) of financial support to German firm CureVac this week in its efforts to support the development and manufacture of a potential vaccine to treat the novel coronavirus (COVID-19). At the time of writing, the disease – labelled as a pandemic by the World Health Organization (WHO) – has killed 8,247 globally.

mRNA and COVID-19

CureVac is not alone in developing a vaccine based on messenger RNA.

This week, a Phase I study evaluating Moderna Therapeutics' investigational mRNA vaccine mRNA-1273 began at Kaiser Permanente Washington Health Research Institute (KPWHRI) in Seattle.

Although such vaccine is not expected to be approved for use within the next six months, production technology will enable rapid production of billions of doses (1 dose = 5 µg).

More about current research: https://bioprocessintl.com/bioprocess-insider/global-markets/one-billion-doses-curevac-gains-88m-to-support-capacity-for-covid-19-mrna-vaccine/?utm_source=hs_email&utm_medium=email&utm_content=84975731&_hsenc=p2ANqtz--joZKsK9FDEazVeMcMgYfK74i9FL7uFJE9bQnff3K0tGbQ7z6zlwCXBFB_w7NAFZdv7ckHViKbOgsOnEYERuvKA01rw&_hsmi=84975731/

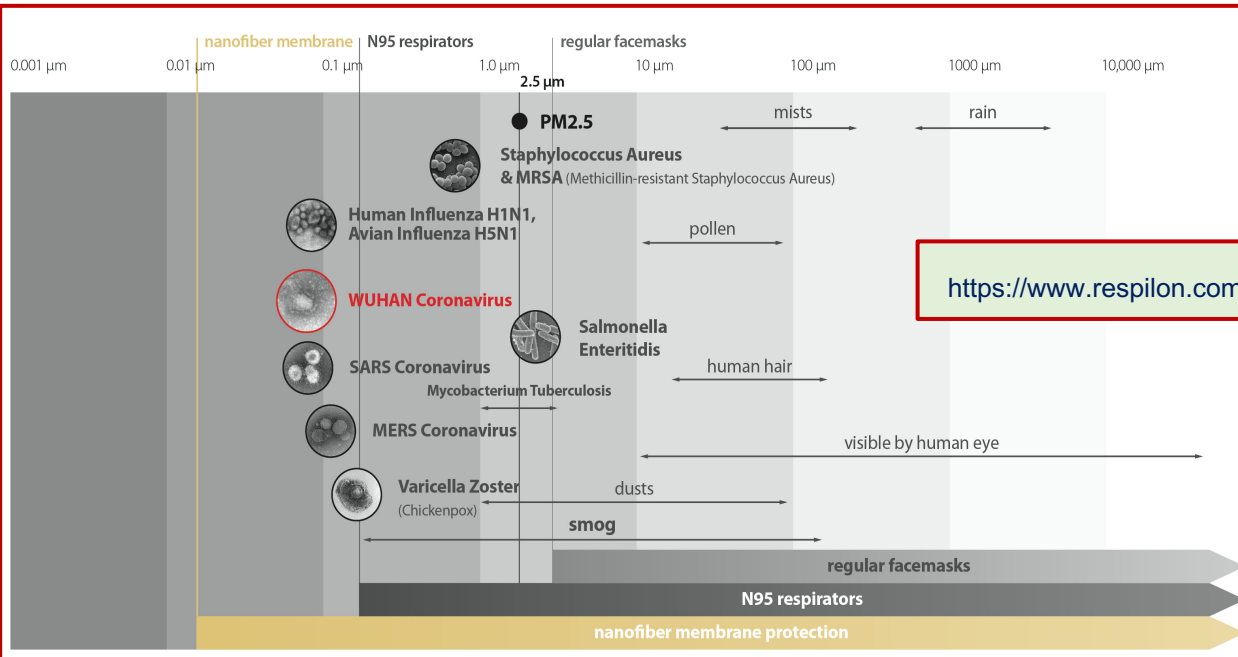
Some practical notes on everyday problems

1. There are no clear guidelines from the relevant government agencies on how to deal with being in an "auto-guarantee" home, for example, if you have a feverish condition and you don't know anything about contact with a potential coronavirus carrier. It is most likely the so-called "cold" or "ordinary" flu, but with some probability, unfortunately, it can also be a coronavirus infection.

So let's take care of our health as we do when we get a "flu-like" infection - each of us has individual preferences here. However, do not use **ibuprofen** (or ibuprofen-containing medicines) to lower your fever and reduce inflammation. Rather, we use **paracetamol**, which has similar anti-fever and analgesic effects. For more unidentified reasons, ibuprofen, like some anti-diabetes drugs and antihypertensives from the so-called prils (e.g. captopril) and sartans (e.g. losartan) are likely to increase the expression of the converting enzyme on the surface of cells, facilitating the entry of the virus into the lung epithelial cells as well as the epithelium of other tissues. It should be emphasized, however, that what was written above is not completely certain and the problem is still discussed in the scientific literature (for more see, e.g. <https://www.medexpress.pl/czy-ibuprofen-oraz-niektore-leki-na-nadcisnienie-i-cukrzyce-moga-zaszkodzic-zakazonym-koronawirusem/76773/>).

In the event of more severe symptoms suggesting a coronavirus infection, follow the procedures defined by the Ministry of Health.

What masks can protect us from viruses and what about disinfectant liquid ?



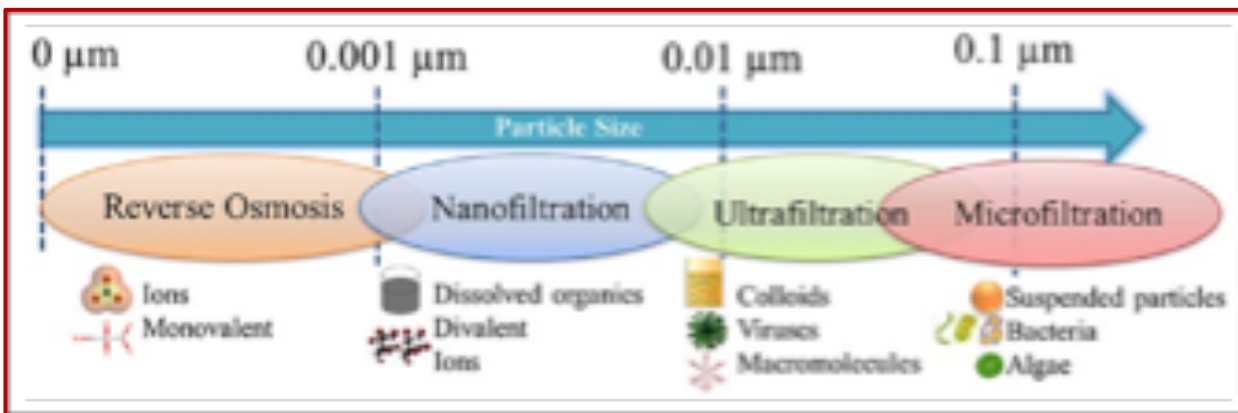
2. We do not share the opinions of government agencies regarding the practical effectiveness of using masks or half-masks. So that the mask can protect us from viruses, it is best if it is sewn from a suitable nanofiber membrane, which passes air molecules and does not pass nanoparticles of virus size. On the left there are two reference sources of information on this subject. As far as conventional masks are concerned, they should be category FFP3 as far as possible, ultimately FFP2.

Regardless of the type of mask/half mask, the complementary carbon filter or active carbon layer always increases its functionality.

Another thing is that the market lacks masks. However, remembering that capitalism can be so effective that for a person who falls into the abyss, it can quickly sew and deliver a parachute, we hope that the situation regarding masks will change.

3. As for the lack of disinfectants, you don't have to wait until Orlen, at the request of the government, spills alcohol with additives into plastic bottles.

Buy ½ liter of spirit and a bottle of distilled water at a gas station. In a smaller container, prepare a mixture of spirit and water in a 4: 1 volume ratio. In this way you will get an alcoholic 80% disinfectant solution (recommended concentration 70-90%). You can add a small amount of some fragrance, cosmetic.



F. Yalcinkaya, *A review on advanced nanofiber technology for membrane distillation*, Journal of Engineered Fibers and Fabrics, 14, 1-12 (2019)

4. Avoid air conditioning systems, especially in large buildings. There are data indicating that the source of MERS viruses (2012-2017, Arab countries) were probably camels, and then the virus began to propagate in high-rise buildings, including through air conditioning systems. Another example is cruise ships. Let's just open windows, which should be more secure.

5. If you have one half-mask (e.g. single-use mask) at all, the situation is difficult but not hopeless. In a difficult situation, it is better to have a single-use, sterilized mask than none.

Suggestion - for sterilization we use UV lamps or sources using UV diodes. Currently, there are many types of small and inexpensive (100-300 PLN) sterilizing devices, used, among others in cosmetic services. Because proteins and nucleic acids absorb around 260 nm and below, the use of sources radiating in this area, or at lower wavelengths, will damage viral macromolecules. An example could be the so-called UV-C sources radiating around 252 nm. On the Internet you can find a number of companies selling such equipment. An example device below. Used masks or gloves can be temporarily stored in plastic food bags, closed with a plastic zipper. We will not propose here military procedures for applying and removing face masks and inserting them in a sterilizing device. Imagine that the mask on both sides is just dirty, and touching them with bare hands should be avoided.



Good luck
P.G. & B.L.