

Coronaviruses belong to a large family of RNA viruses that cause many diseases in humans - from the common cold to severe acute respiratory syndrome (SARS).

Typical symptoms of RNA viruses include fever, cough, or shortness of breath. Pneumonia often occurs, and in severe cases, with a weak immune response to infection, respiratory arrest may occur.

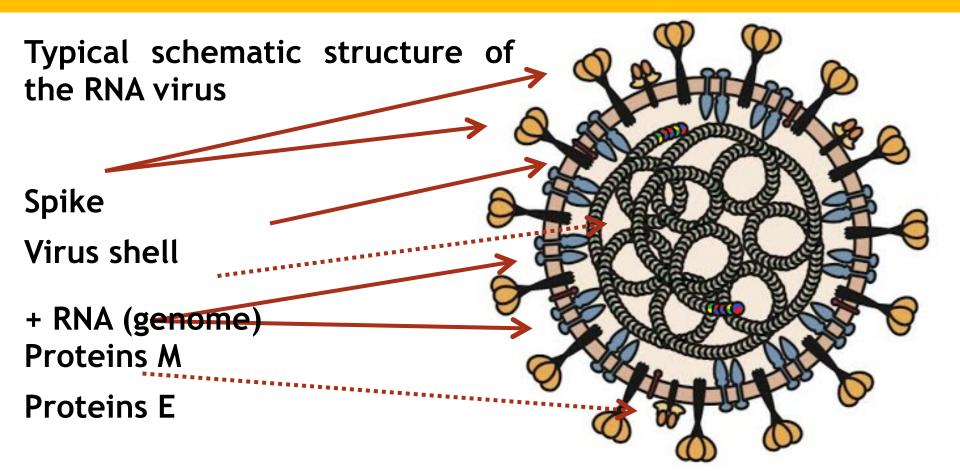
In some patients, the function of other organs may be impaired, but most often kidney failure or septic shock develops.

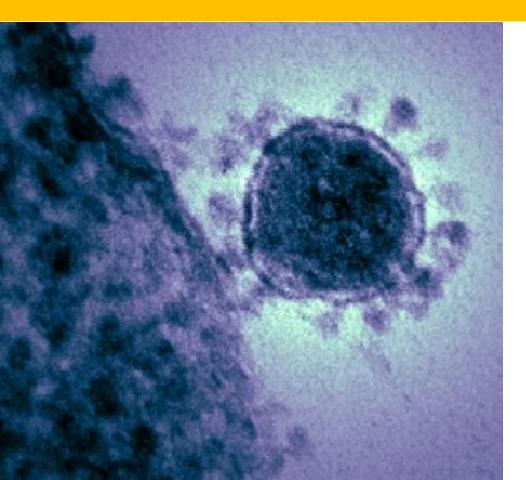
In most cases, RNA viruses cause complications, more severe course or progression of diseases, including the manifestation or progression of previously existing diseases, in people with weakened immunity or the progression of chronic diseases, especially in the elderly.

This mainly concerns people with cardiovascular diseases, diabetes, chronic respiratory diseases, hypertension or people with oncology.

However, it is not uncommon for people infected with the virus to almost never experience any serious or specific symptoms. In these cases, early detection of an RNA virus infection is not always possible. However, symptoms of infection may occur within 14 days.

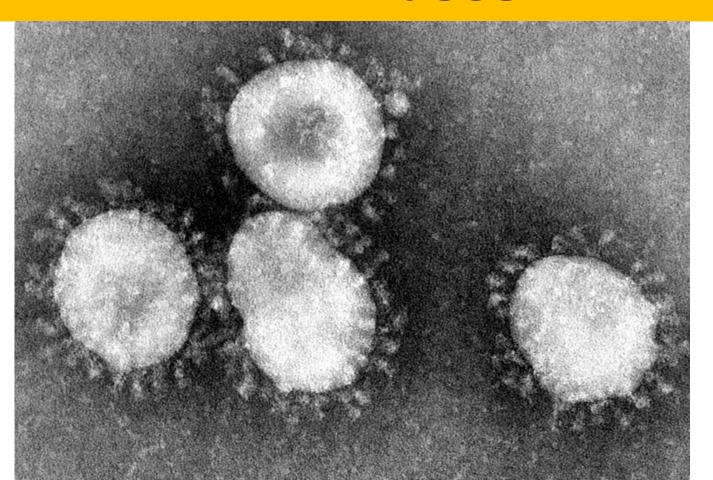
The use of standard and specific immunostimulating and immunomodulating procedures, methods and means of preventing the development of infection (prevention), in my opinion, more effective than treating an existing infectious infestation.





Attachment of the RNA virus with its spikes to the outer surface of the cell membrane of the host cell (via ACE2 protein)

At this stage, the virus is still vulnerable to immune cells.

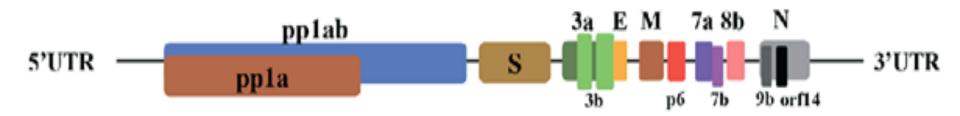


RNA viruses interact with cells through Spike proteins (the so-called "spikes" on its surface).

The genome of the virus consists of four components:

- 1. Proteins S1 and S2;
- 2. Component ectodomain;
- 3. Transmembrane anchors;
- 4. Short intracapsid tail.

Novel Coronavirus Virus Genome (2019-nCoV)

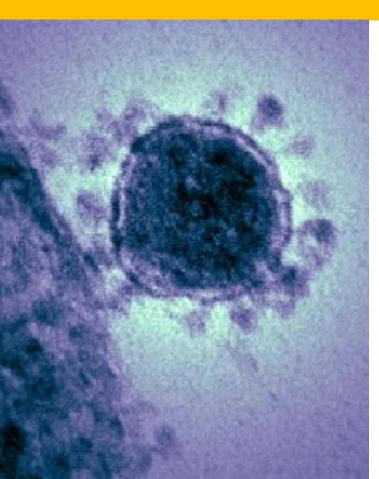


Proteins pp1ab and pp1a are non-structural cleavage products that are involved in the transcription and translation of the viral genome:

- **S** this is the spike protein of the virus (Spike)
- E this is the membrane protein
- **M** this is the membrane protein
- **N** this is the nucleocapsid proteins

It is the ectodomain of the Spike protein that binds to the RBD domain of the ACE2 cell receptor. RBD (RNA Binding Domain) is the central nucleolin domain that contains four conserved RNA binding domains, which in turn provide further, specific interaction with nucleic acid sequences.

In terms of amino acid composition, the Spike 2019-nCoV protein is closest to the SARS-CoV protein. Their similarity corresponds to ~ 76.5%.



The ability of coronaviruses to penetrate the host cells and cause infection in the body is mediated by the interaction of the thorn of the virus with the surface receptors of certain human cells.

It is important to note that 2019-nCoV (Novel Coronavirus) and COVID-19, the viruses that caused the latest epidemiological outbreak, use the same ACE2 cell entry receptor as SARS-CoV.

Thus, the human ACE2 protein is, as it were, the main "gateway" for the entry of RNA viruses into the host cell.

Virus variations can cause structural rearrangements that allow new and possibly even faster and denser subsequent interactions with ACE2.

The 2019-nCoV coronavirus has been suggested that a single N501T mutation in a Spike protein is related to SARS-CoV-2, but with significantly increased binding to ACE2.

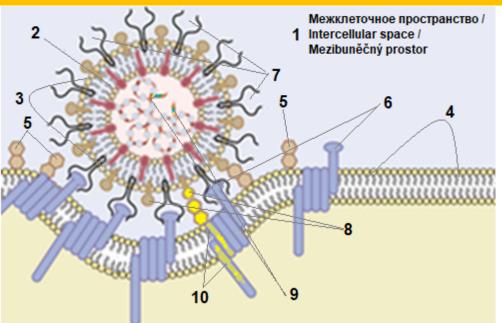
Given this, it is unlikely that the SARS spike protein mutated during the 2002-2004 epidemic, so that only in 2019-2020, it would be better to start binding to only certain receptors on the human cell surface.

Coronavirus Spike proteins are trimers of type I transmembrane protein that protrude from the surface of the virions.

The subunit S1 of the ectodomain mediates the binding of the virion to the receptors of the surface of the host cell through its receptor-binding domain (RBD) - the binding bridge.

Subunit S2 fuses with both the host cell and viral membranes, creating dramatic structural changes and mutations.

The penetration of the virus into the cell using S protein:

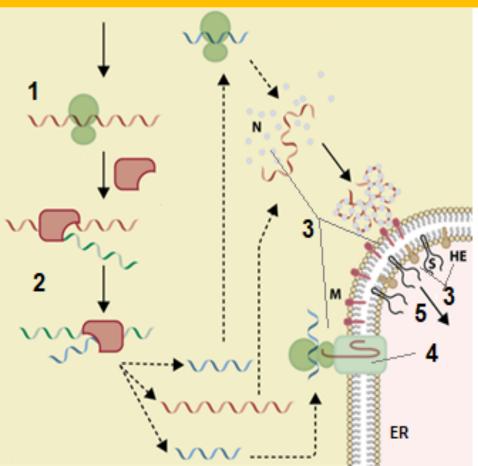


- 1. Intracellular space
- 2. Virus
- 3. Virus envelope
- 4. Cellular
- 5. N-acetyl neuraminic acid
- 6.ACE2 receptor (ACE2 coronavirus receptor is an angiotensin-converting enzyme II receptor that is found in the cells of the pulmonary alveolar epithelium, small intestine enterocytes, in endothelial cells of arteries and veins).
- 7. Maceous processes (S-surface glycoprotein, penetrates into the cell).
- 8. E envelope proteins (assembly and exit)
- 9. Genome + RNA approximately 30,000 nt long
- 10. Port or channel of penetration

Explanation: + RNA contains a cap structure and a polyA sequence. Capping is necessary to initiate protein synthesis, and the initiating nucleotide is recognized by the ribosome only if a cap is present.

Also, the cap structure is a protection against rapid degradation. The polyA sequence is necessary so as not to be recognized by intracellular immune response systems that destroy RNA without such structures.

Cellular reproduction of RNA viruses



- 1.1. Since coronaviruses have one positive RNA genome with chains, they can directly produce their proteins and new genomes in the cytoplasm. First, the virus synthesizes its RNA polymerase, which only recognizes and produces viral RNA. This enzyme synthesizes the negative chain using the positive chain as a template.
- 2. Subsequently, this negative chain serves as a template for transcription of smaller subgenomic positive RNAs that are used to synthesize all other proteins. In addition, this negative strand serves to replicate new positive strand genomic RNAs.
- 3. Protein N binds genomic RNA, and protein M integrates into the membrane of the endoplasmic reticulum (ER), like the envelope proteins S and HE. After binding, the assembled nucleocapsids with spirally twisted RNA are released into the ER lumen and enclosed in the membrane.
- 4. Trans-locator.
- 5. The resulting viral offspring is transported by Golgi vesicles to the cell membrane and exocytosed into the extracellular space.

The Novel Coronavirus virus genome (2019-nCoV) has four unusual protein insertion sequences.

The comparison showed that they are not present in any other strains of coronavirus, but show identity / similarity with rapidly changing amino acid sequences (they differ by a quick change in the length of the amino acid sequence), which leads to a significant increase in the level of replication of the virus and indicates an increase in its adaptability.

These inserts add extra flexibility to RBD by forming a hydrophilic loop that provides a host-virus interaction with greater infectivity. It is worth noting that their presence "is unlikely to be random in nature."

So, it can be speculated that 2019-nCoV (SARS-CoV-2) was "specially designed" with additional sequences of codon coding region inserts.

However, given that these inserts appear in the hypervariable regions of the protein and have a length of only 6 residues, it is still possible to assume that they could arise naturally.

Therefore, in the future, to confirm or refute one of the above options, various comprehensive studies of cellular immune responses for these strains of coronaviruses 2019-nCoV (SARS-CoV-2), COVID-19 will be required.

The coding regions consist of codons that follow directly one after another in sequences of three nucleotides, each of which corresponds to a specific amino acid in the genetic code i.e. the beginning and end of protein synthesis. Coding regions begin with a start codon and end with one of three stop codons.

Reading of the codon sequence and assembly on its basis of the amino acid sequence of the synthesized protein molecule is carried out by ribosomes with the participation of transport RNA in the translation process.

In addition to coding for proteins, portions of coding regions can also serve as control sequences.

The survival strategy of all viruses is based on "avoiding" the host's adaptive immune response. To do this, they have a set of special mechanisms. In particular, avoiding the VTLT immune response is based on preventing the recognition of corresponding epitopes by immune cells.

An epitope, or antigenic determinant, is part of an antigen macromolecule that is recognized by antibodies as well as B-lymphocytes and T-lymphocytes of the immune system.

Like other Spike coronaviruses, the 2019-nCoV protein (SARS-CoV-2) induces a series of neutralizing antibodies, causing disturbances in the response of cytotoxic T-cell immunity.

Cytotoxic T cell immunity

Cytotoxic T-cell immunity is important in preventing the development of viral infection and mitigating its severity.

The regulation of the mechanisms of induction of virusspecific CD8 + T-lymphocytes (VTTL) in humans contributes to the improvement of prophylactic effects against infection.

CD8 + play an important role in controlling viral infections through the cytolytic destruction of infected cells, followed by their elimination from the body.

Cytotoxic T cell immunity

With respect to influenza infection, the role of VTsTL in reducing the severity of the disease and preventing infection, as in experimental experiments in mice, has been proven (Taylor P.M., Askonas B.A. Influenza nucleoprotein-specific cytotoxic T-cell clones are protective in vivo. Immunology. 1986), so when volunteers become infected (McMichael A.J., Gotch F.M., Noble G.R., Beare P.A. Cytotoxic T-cell immunity to influenza. N. Engl. J. Med. 1983).

Cytotoxic T cell immunity

The main targets for VTsTL are immunodominant epitopes of the internal proteins of RNA viruses present on the surface membrane of infected cells.

Nevertheless, it must be emphasized that although neutralizing antibodies can prevent the penetration of the virus, the body also needs T helper cells to produce specific antibodies, as well as to recognize and destroy infected cells, especially in the lungs of infected people.

Interleukin-2 (IL-2)

Interleukin-2 (IL-2) is a peptide of one of the types of cytokines, which is a mediator of inflammation and at the same time a mediator of immunity.

It is produced by T cells in response to antigenic and mitogenic stimulation.IL-2 is necessary for the proliferation of next generations of T cells and other processes that regulate the immune response.

Interleukin-2 (IL-2)

Interleukin-2 is the main cytokine in the family of interleukins IL-4, IL-7, IL-9, IL-15, IL-21.

All of these interleukins act via the IL-2 alpha receptor (CD25) or the IL-2 beta receptor (CD122).

Activation of IL-2 is vital for the development and functioning of lymphocytes.

Interleukin-2 (IL-2)

Interleukin-2 also activates signaling pathways:

- 1.Ras / MAPK (survival, proliferation and increased cell motility);
- 2.JAK / Stat (gene expression, which stimulates blood renewal, the emergence of immune cells and fat cells, participates in the process of cell division and death, plays a major role in the transmission of cytokine receptor signals);
- 3.PI 3-kinase / Akt (growth, proliferation, differentiation, motility and survival of cells, as well as regulation of intracellular metabolism / is especially important in oncology).



Dietary supplement <u>PREVENTAVIR</u> (another name for the product is IMMUBOO supplement) contains 100% natural ingredients that have undergone exclusive double extraction technology from medicinal mushrooms and brown poppy root with the addition of PROVEOTICS probiotics.

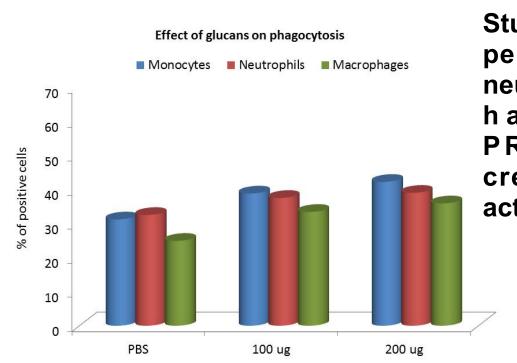
The mixture contains: Grifolinacid, Triterpenes, Crystalline amino acids Ifidobacterium longum, Streptococcus thermophilus, a mixture of Lactobacillus (acidophilus, bulgaricus, rhamnosus, fermenti, helveticus, paracase)

www.bioono.com

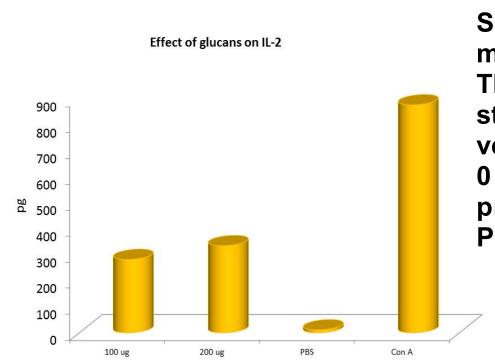


The dietary supplement <u>PREVENTAVIR</u>, (supplement IMMU BOO) was tested in a laboratory of the Department of Pathology at the University of Louisville, Kentucky, USA.

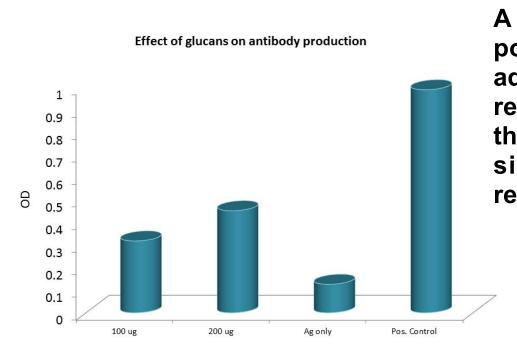
The experimental data obtained during the studies allowed us to conclude with confidence that glucans of the dietary supplement PREVENTAVIR are highly active immunostimulants.



Studies of phagocytosis (both in peritoneal macrophages and in neutrophils and blood monocytes) have shown that taking PREVENTAVIR supplements creates significant stimulating activity in all types of cells.



Similar results were obtained when measuring the production of IL-2. The production of IL-2 without any stimulation in the body is usually very low (sometimes even equal to 0), therefore, the observed production of IL-2 when taking PREVENTAVIR is very significant.



A study was conducted on the possibility of stimulation by the addition of PREVENTAVIR antibody response. It has been confirmed that taking an already daily dose significantly improved antibody response (compared to Ag).

PREVENTAVIR - study findings

The immunostimulating activity of the test sample for cellular immunity (phagocytosis) was confirmed. An increase of 30–40% was observed in comparison with the control sample without the use of an additive.

The immunostimulating activity of the test sample on humoral immunity was confirmed. There was a 30–40-fold increase in antibody production and secretion of IL-2, compared to the standard response.

A 200-300% increase in antibody production was confirmed in comparison with the control Ag. A slight increase in own stem cell production by 5-10% was confirmed !!!

However, statistically it is difficult to give a proper assessment due to the short testing period.

Department of Pathology
University of Louisville School of Medicine
Date: 28 day of October, 2019

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Coronavirus Information

"COVID-19 Medial Hysteria" is more like an information epidemic.

We are told that the epidemic is growing uncontrollably. Every day, the numbers of statistics (infected and dead) change.

The following will be the official information and in some places my own opinion or explanation.

Everyone can make conclusions himself!

Coronavirus Information

But first, I'll ask you to pay attention in advance to certain highlighted dates, statistical numbers in them and / or events accompanying them. So. It all started on December 12, 2019 in Wuhan, Hubei Province, China (Wuhan City, Hubei Province of China).

An outbreak of infection caused by an unknown virus has occurred. In five patients, at an early stage of the outbreak, full length genome sequence samples were obtained for the new virus.

They were almost identical to the sequences for SARS-CoV.

Coronavirus Information



The highlighted virus was given the name Novel Coronavirus (2019-nCoV) and the history of the epidemic has begun.

However, official statistics from the World Health Organization (WHO) are only available from January 21, 2020.

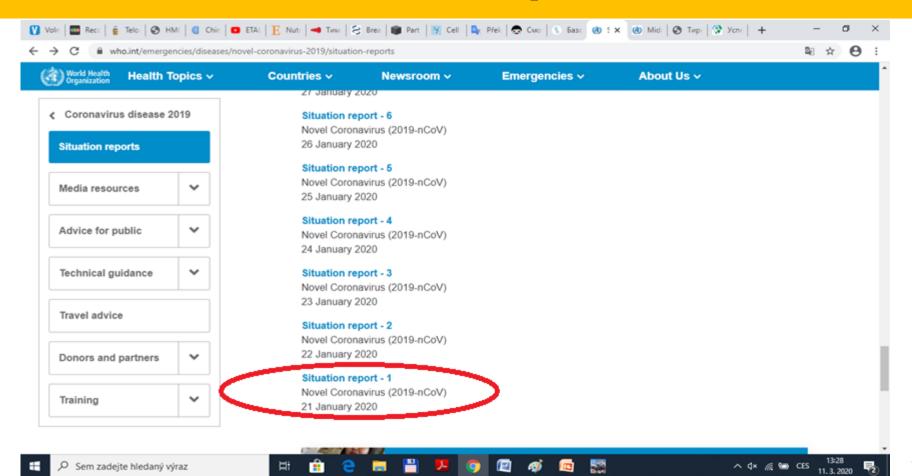
Coronavirus Information

11.02.2020

WHO was "not satisfied" with the Chinese name of the virus and officially adopted its name, both the virus and the name of the epidemic itself - COVID-19?

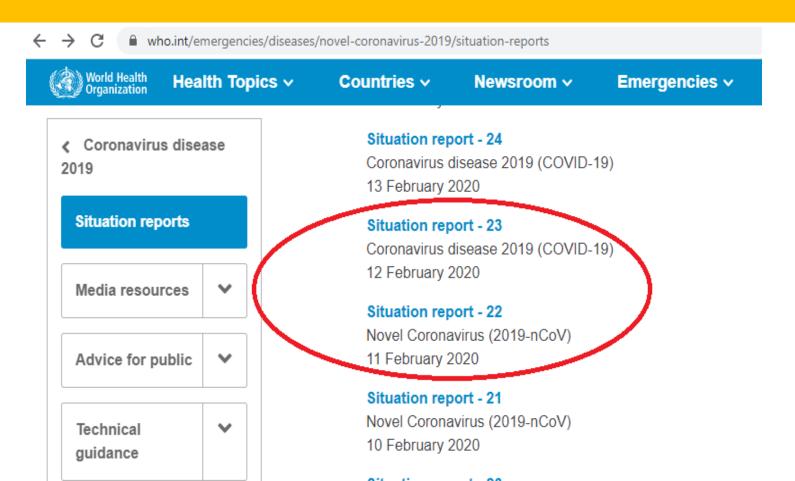
[https://www.who.int/dg/speeches/detail/who-director-general-s-remarks-at-the-media-briefing-on-2019-ncov-on-11-february-2020].

Novel Coronavirus epidemic or ...



Sem zadejte hledaný výraz

... COVID-19



The total number of confirmed cases in the world of Novel Coronavirus (2019-nCoV)

Datum / Дата	Confirmed cases / Подтвержденные случаи		
21.01.2020	282		
22.01.2020	314		
Datum / Дата	Confirmed cases / Подтвержденные случаи		
	China / Китай	Total / Bcero	
23.01.2020	571	581	
24.01.2020	830	846	
25.01.2020	1297	1320	
26.01.2020	1985	2014	
27.01.2020	2761	2798	
28.01.2020	4537	4593	
29.01.2020	5997	6065	
30.01.2020	7736	7818	
31.01.2020	9720 9826		
Total deaths / Общее количество смертей до 31.01.2020 213			

Datum / Дата	Confirm ed cases / По	Deaths / Случаи смерти	
	China / Китай	Total / Bcero	
01.02.2020	11821	11953	259
02.02.2020	14411	14557	304
03.02.2020	17238	17391	361
04.02.2020	20471	20630	425
05.02.2020	24363	24554	491
06.02.2020	28060	28276	564
07.02.2020	31211	31481	637
08.02.2020	34598	34886	723
09.02.2020	37251	37558	812
10.02.2020	40235	40554	909
11.02.2020	<mark>42708</mark>	<mark>43103</mark>	<mark>1017</mark>

13.02.2020
One day after renaming, an inexplicable increase in deaths occurs ...

Check for yourself the average increase in deaths per day and you will see that 02/13/2020 is very strangely different from these deaths before ... and even after that date.

Total confirmed cases worldwide Coronavirus disease 2019 (COVID-19)

Datum / Дата	Confirm ed cases / По	одтвержденные случаи	Deaths / Случаи смерти
	China / Китай	Total / Bcero	
12.02.2020	<mark>44730</mark>	<mark>45171</mark>	<mark>1114</mark>
13.02.2020	46550	46997	1368
14.02.2020	48548	49053	1381
15.02.2020	50054	50580	1524
16.02.2020	51174	51857	1666
17.02.2020	70635	71429	1772
18.02.2020	72528	73332	1870
19.02.2020	74280	75204	2006
20.02.2020	74675	75748	2121
21.02.2020	75569	76769	2239
22.02.2020	76392	77794	2348
23.02.2020	77042	78811	2445
24.02.2020	77262	79331	2595
25.02.2020	77780	80239	2666
26.02.2020	78191	81109	2718
27.02.2020	78630	82294	2747
28.02.2020	78961	83652	2791
29.02.2020	79394	85403	2838
01.03.2020	79968	87137	2873

Noteworthy is the following date 02/17/2020On this day, not mortality is increasing ... but the number of confirmed cases of infection is growing incredibly and inexplicably ...

This coincided with the statement of the previous day about "Waiting for a large possible growth of the COVID-19 epidemic (including in Europe)"

19.02.2020 Total mortality is kept at 2.3%. The highest mortality rate is found in people over 80 years old - 14.8%.

In people from 70 to 80 years, mortality is - 8%.

In the group of people 10-40 years old, mortality is 0.2%.

Not one child aged 0-9 years has died.

03/01/2020

The number of new cases of infection with COVID-19 coronavirus outside of China for the first time exceeded the number of cases in China itself.

From 02.03.2020 the statistics tables are presented differently (mortality over the past 24 hours in China is shown, and the development of COVID-19 outside of China is shown in more detail)

ChinaMortality ≈ 3,7%

Datum / Дата	In last 24 hours / За последние 24			Cumulative /	
	часа			Накопительное значени	
Total / В общем	Confirmed	Suspected	Deaths	Confirm ed	Deaths /
	cases /	cases /	/	cases /	Случаи
	Подтвержд	Случаи	Случаи	Подтвержденн	смерти
	енные	подозрения	смерти	ые	
	случаи			случаи	
02.03.2020	206	141	42	80174	2915
03.03.2020	130	129	31	80304	2946
04.03.2020	120	143	38	80422	2984
05.03.2020	143	143	31	80565	3015
06.03.2020	146	102	30	80711	3045
07.03.2020	102	99	28	80813	3073
08.03.2020	46	84	27	80859	3100
09.03.2020	45	60	23	80904	3123
10.03.2020	20	36	17	80924	3140

Countries, territories or areas outside China

Datum / Дата	Confirm ed cases /	New cases	Deaths /	Total new deaths / Общее
	Подтвержденные	/ Новые	Случаи	количество новых
Total / В общем	случаи *	случаи	смерти	смертей
02.03.2020	8774	1600	128	24
03.03.2020	10565	1792	166	38
04.03.2020	12669	2103	214	48
05.03.2020	14759	2089	266	53
06.03.2020	17481	2727	335	69
07.03.2020	21114	3633	413	78
08.03.2020	24727	3610	484	71
09.03.2020	28673	3948	686	202
10.03.2020	32778	4105	872	186

By early March, deaths from COVID-19 outside China ≈ 1.7%

Incidence / Mortality

Among healthy people under the age of 50, the mortality rate from Novel Coronavirus (2019-nCoV) / COVID-19 is quite low.

And in older patients, the mortality rate is much higher. Available data indicate that the mortality rate in older people and people with cardiovascular diseases, diabetes and cancer, as well as in patients with immunodeficiency syndrome, is higher and ranges from 9 to 19% (information from a WHO briefing on 03/09/2020)

Incidence / Mortality

The percentage of deaths from the anamnesis

Anamnesis	Mortality	
Cardiovascular diseases	19,5%	
Diabetes	16,3%	
Chronic respiratory disease	15,3%	
Hypertension	10,4%	
Oncology	8,6%	

Other: 29,9%

Comparison

In the period 2017-2018.

About 650,000 people died from common flu in the world.

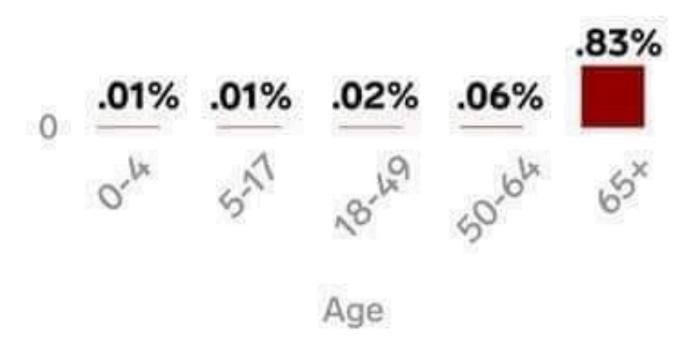
And it was not a pandemic - it was a common flu. In the USA, during the fall-spring 2019-2020 (until early March), 8,200 people died from RNA viruses.

And how much is from COVID-19?

Infected 62 people, died - 0 ...?

Comparison

Age-specific incidence statistics for COVID-19



SARS/TOPC or MERS-CoV

To date, mortality from Coronavirus COVID-19 (about 5.4%) is lower than, for example, from SARS / SARS (SARS, which arose in 2003).

Then mortality was 9.6%. Mortality in Coronavirus 2012 Middle East respiratory syndrome (Middle East respiratory syndrome coronavirus MERS-CoV) was 36%.

COVID-19 - no panic!

For most people, COVID-19 can be just an infection, albeit an aggressive but not fatal infection. However, with a weak immune response, more serious complications can arise, including life risks and death.

This is especially true for older people as well as people at risk with chronic diseases of the cardiovascular system, respiratory diseases or diabetes.

COVID-19 - no panic!

It must be remembered that if you are in an area where COVID-19 infections have indeed been confirmed, you should be more serious about the potential risk of infection and take appropriate measures to protect yourself and your family, including maximizing the potential for preventive measures.

COVID-19 - solidarity and responsibility

Each person infected with seasonal flu can infect approximately 1.3 other people. SARS-CoV-2 (the virus that causes COVID-19) infects about three times as many people (according to current spread estimates, up to 4 people).

This number of infections is called the reproductive factor, or "R0." This propagation speed allows the current coronavirus to multiply very quickly. Such breeding between people and their infection can lead to an overload of an already busy healthcare system.

COVID-19 - solidarity and responsibility

So, even if you yourself are not at a high risk of morbidity, from a public point of view and solidarity it is necessary to take measures that will prevent the spread of the virus.

It must be borne in mind that the rapid increase in the number of sick people can lead to an overload of the health system, as is happening now in Italy.

COVID-19 - solidarity and responsibility

Do not be a person who spends medical and hygiene resources that someone may need more than he needs. This is a matter of ethics and humanity.

We must minimize the spread of the virus so that health care resources (from diagnosis and treatment, to respirators and oxygen devices) are available to the people who need them most.

Slower distribution will save many lives, because a nonoverloaded health system will be able to provide timely assistance in full to those who need it most.

Keep a minimum distance of 1.5 meters from people who have a persistent cough, runny nose and / or fever. If possible, do not touch your eyes, nose, and mouth with your hands before handling your hands.

So, as the hands touch many surfaces on which the virus may be present. If you touch your eyes, nose, or mouth with your hands, you can transfer the virus from your skin to your body.

Follow the rules of respiratory hygiene. When coughing and sneezing, cover your mouth and nose with a tissue, handkerchief, or hand.

This virus, as already mentioned, has a high reproductive factor (R0) and a high prodromal (asymptomatic or incubation) period - which is about 14 days.

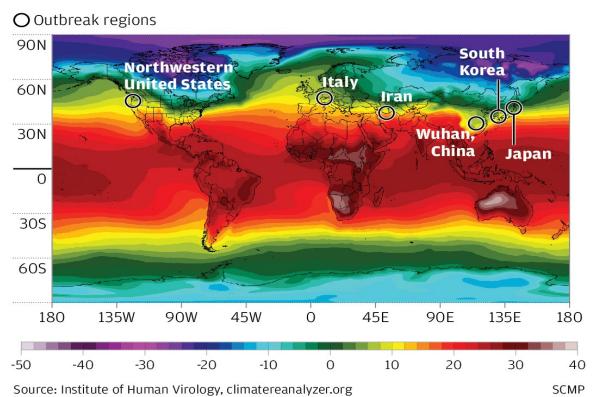
Do not forget that some people can be carriers of RNA viruses without symptoms.

Apparently, the coronavirus can go into a "sleeping" or inactive mode.

However, in the fall, he can continue all over again and amaze new people.

COVID-19

Severe Covid-19 outbreaks



The largest foci of COVID-19 development so far have arisen in the socalled cooler areas of the world. However, one must understand the virus does not respond to heat, but to the power of direct sunlight (body temperature is about 37 ° C and the virus easily survives with it)

The problem of COVID-19 is not so much mortality as the overall impact of an infectious outbreak.

Although other diseases can be more fatal, the combination of the reproductive factor (R0) and the susceptibility of a population where immunity is an important factor cannot be underestimated.

It must be borne in mind that this SARS-CoV-2 strain (the virus that caused Novel Coronavirus (2019-nCoV) / COVID-19) is completely new, so no one is safe.

There is no clinical trial of a valid vaccine for this strain of the virus. According to experts, its development, verification and implementation will require enough time.

Estimated dates not earlier than the 1st quarter of 2021. So while the best protection remains - the prevention of the immune system, hygiene, alcohol-based disinfection (70-90%).

However, it must be understood that disinfectants can only slow down the virus, but not make it completely powerless.

Most likely, in March and April 2020, the pandemiological situation will not change. Perhaps in May and June the epidemic will begin to decline.

But given that the vaccine will not be before 2021, several more epidemiological outbreaks may well occur. How the coronavirus behaves further is a big question. Nevertheless, we can do prophylaxis against it or other RNA viruses.

For example, using **PREVENTAVIR**.



Remember that panic and fear do more harm than the coronavirus itself.

We must be realistic and at the same time be prepared for various possible consequences, correctly understand the big picture and the reality behind it and adequately respond by taking reasonable actions.

I emphasize just reasonable actions in order to minimize the risks that have already arisen.

I WISH ALL HEALTH AND STRENGTH!