COVID-19 meta-analysis

Study on the state of knowledge on the pathomechanism of COVID-19, as of mid-April 2020

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Question:

How exactly does the SARSCoV2 virus damage the human body when it triggers the disease COVID-19?

Lead author, motivation and methodology:

The author Peter Dirscherl is a doctor.
The in-depth study of scientific sources and at the same time intensive observation and discussion of all publications available to him in the media and on various social media channels on the subject of “new coronavirus” with a scientific background enable the author to take a well-founded position.
The aim of the study is to optimize the way the coronavirus pandemic is dealt with in order to ultimately be able to contribute as far as possible to preventing further infection of the population. It is very important to be familiar with the first reports and experiences, especially from China, although these sources have unfortunately often been retracted from being publicly available in the meantime.
The method is descriptive and there is no meticulous citation of sources, because the time required for this appears disproportionately high under the existing time pressure, with a dynamically spreading epidemic, and because recipients should be well able to do research in the age of the Internet to put up postulates and to review sources for the research results mentioned.

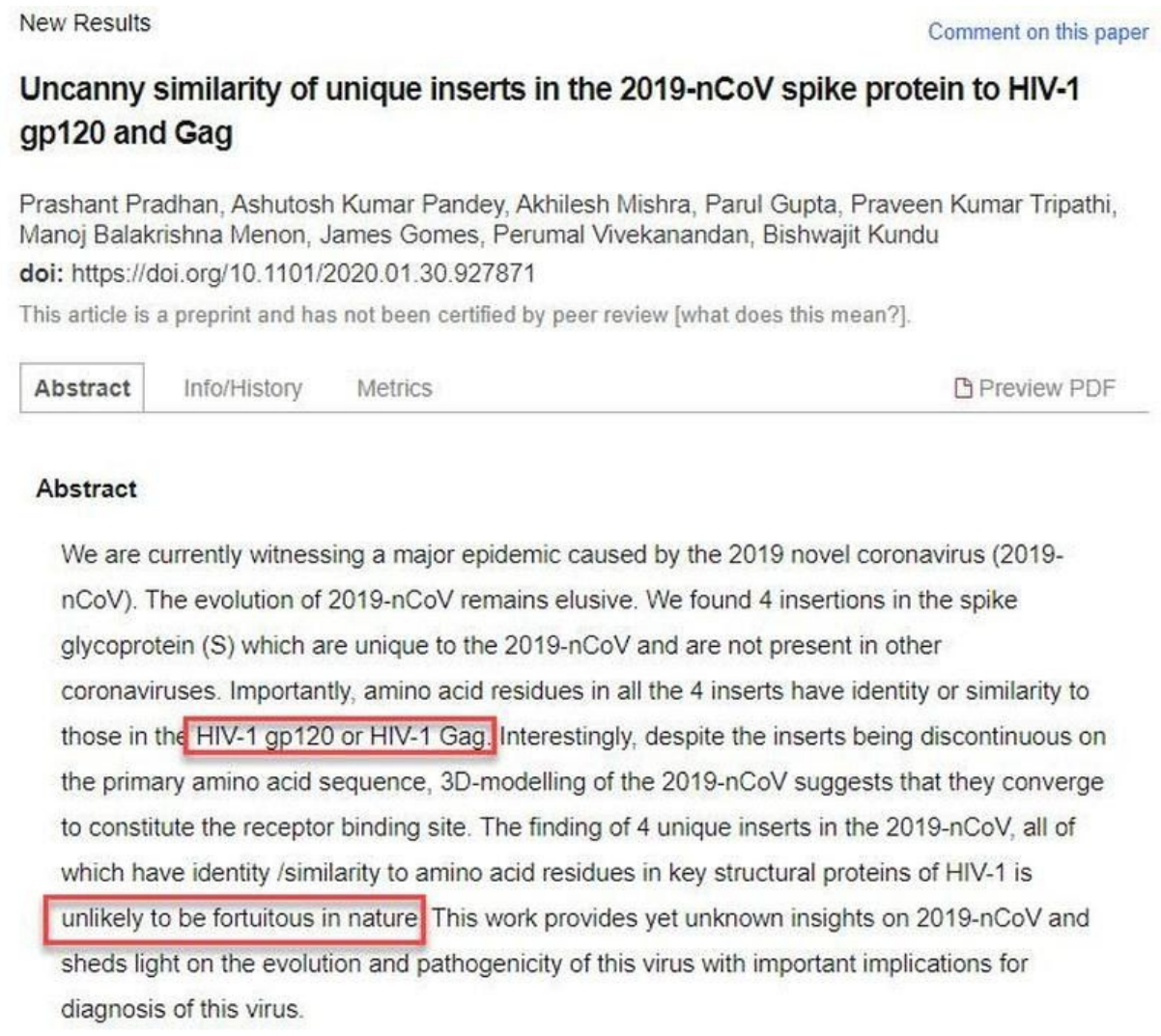
Main characteristics of SARSCoV2:

Like all corona viruses, the SARSCoV2 virus is a zoonotic pathogen that can reproduce in humans as well as in various mammals and birds. Mutual infection is possible through the virus reservoirs in different animal species.

The virus has an extremely high affinity for human ACE2 receptors on cell surfaces and, after binding to the angiotensin converting enzyme II, reaches the human body cells via these receptors, where it can multiply. Due to the high binding affinity, a very small amount of virus compared to other human pathogenic viruses is sufficient to trigger an infection.

SARSCoV2 is sensitive to alcohol and heat and becomes harmless when heated for several minutes from 70 degrees Celsius. Recent research results that contradict these early findings by Taiwanese scientists appear to be poorly validated. At normal room temperature, the virus can persist infectiously on surfaces for up to several hours. Previous studies have shown that similar coronaviruses can remain infectious in dried saliva for several weeks.

The virus genome is similar to the corona virus genome known in bats and pangolines.
A group of Indian scientists led by Prashant Pradhan published a study as a preprint on January 30, 2020, which concluded that more than 10% of the genetic sequences of SARSCoV2 have no similarities to known coronaviruses, but instead have similarities to sequences of the HIV virus, what prompted these researchers to postulate the thesis that it was a synthetically designed bio-weapon.



New Results

Comment on this paper

Uncanny similarity of unique inserts in the 2019-nCoV spike protein to HIV-1 gp120 and Gag

Prashant Pradhan, Ashutosh Kumar Pandey, Akhilesh Mishra, Parul Gupta, Praveen Kumar Tripathi, Manoj Balakrishna Menon, James Gomes, Perumal Vivekanandan, Bishwajit Kundu

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This article is a preprint and has not been certified by peer review [what does this mean?].

Abstract | Info/History | Metrics | Preview PDF

Abstract

We are currently witnessing a major epidemic caused by the 2019 novel coronavirus (2019-nCoV). The evolution of 2019-nCoV remains elusive. We found 4 insertions in the spike glycoprotein (S) which are unique to the 2019-nCoV and are not present in other coronaviruses. Importantly, amino acid residues in all the 4 inserts have identity or similarity to those in the HIV-1 gp120 or HIV-1 Gag. Interestingly, despite the inserts being discontinuous on the primary amino acid sequence, 3D-modelling of the 2019-nCoV suggests that they converge to constitute the receptor binding site. The finding of 4 unique inserts in the 2019-nCoV, all of which have identity /similarity to amino acid residues in key structural proteins of HIV-1 is unlikely to be fortuitous in nature. This work provides yet unknown insights on 2019-nCoV and sheds light on the evolution and pathogenicity of this virus with important implications for diagnosis of this virus.

This study was initially withdrawn for unknown reasons. In recent weeks, however, signs of the plausibility of the thesis of the Indian researchers have increased.

The pathomechanism(s) of COVID-19:

The virus enters the human body almost exclusively via mucous membranes, but it is theoretically also a sanguine transmission pathway through blood products / products and contaminated needles in i.v. Drug use possible. SARSCoV2 gets into the human body cells through the mouth, throat, nose, and above all also the mucous membranes of the eyes, more rarely also through the anal and genital mucous membranes. The amount of virus initially taken in seems to play an important role in pathogenicity. SARSCoV2 is most commonly transmitted by droplet infection of particles exhaled when speaking or coughing / sneezing. The virus also occurs in smaller particles than aerosol in the air, but then there must be a highly infectious person in the area to allow infection. This transmission path is particularly relevant in hospitals, supermarkets and in public transport, which is why it can be advantageous to wear protective goggles in these places as well as closed protective glasses to protect yourself from infection. Lubricating infections with a fecal-oral transmission path and via the hands also represent a not to be neglected risk of infection. SARSCoV2 is often excreted by stool in infected people and can theoretically also spread via wastewater disposal channels, e.g. about animals or aerosol emissions. Infection through sexual contact with infected people does not appear to be excluded either.
After infection, if the amount of virus is too large to be immediately made harmless by the immune system and there is an increasing virus multiplication by replication in the affected body cells, the first symptoms of COVID-19 usually appear after a few days.

The disease usually begins with an initial respiratory phase with runny nose, sore throat, difficulty swallowing and coughing. Headaches, loss of smell and flu-like muscle and body aches combined with an intense feeling of exhaustion are also common early symptoms. Sometimes digestive complaints with nausea and diarrhea occur. The gastrointestinal route of infection does not seem to play an important role for the initial pathomechanism. It can be assumed that the viruses are mostly made harmless by gastric acid during gastric passage. The pronounced exhaustion is probably related to an incipient systemic immune response. When this intensifies, fever often occurs. If additional breathing difficulties with shortness of breath occur, this usually signals the transition from the first local respiratory illness phase to the second, very dangerous, systemic illness phase.

The dreaded and often fatal “Wuhan pneumonia” is the central complication of an infection with SARSCoV2. If the typical glass bottom-like finding of this pneumonia is visible in chest CT, there is usually also a viremia and the virus gets into blood cells. In particular, the number of leukocytes drops sharply, which contributes to a typical dysfunctional response of the immune system and, with increased local interleukin release in the affected organs, i.e. initially mostly in the lungs, also contributes to significant edema formation. It is not uncommon for cytokine storms and very high fevers to occur as part of the enormous immune balance. The faster a systemic spread of the virus occurs with a severe course of the disease, the less the immune system is able to build up a targeted immune response

using IgG antibodies. This is particularly unsuccessful because CD-4 lymphocytes in particular are affected and can no longer fulfill their function as memory cells.

In the systemic phase of COVID-19, when adult patients usually become ventilators, progressive multi-organ failure quickly occurs, which process is exacerbated by the existing lack of oxygen and by the decay of blood cells and electrolyte shifts. Lack of oxygen and hypokalaemia alone can lead to organ damage. In addition to the reduced oxygen absorption capacity in pulmonary edema and reduced cardiac ejection, the lack of oxygen is also essentially caused by the virus's binding to hemoglobin and the associated functional impairment. The role of associated changes in iron metabolism are still controversial.

The development of pulmonary fibrosis is a serious and frequent complication of patients with severe disease courses, but has also been reported as a late complication in milder courses.
Kidney function is impaired by the deposition of cell decay products and immune complexes, as well as by electrolyte shifts and by direct viral organ involvement, and kidney failure requiring dialysis often occurs.

Heart attack causes cardiomyopathy and pericardial effusion. In addition, hypokalaemia affects the conduction system, which can lead to sudden cardiac arrest.
Inflammation also affects liver function considerably, which can also impair the function of the coagulation system and lead to bleeding or embolism and infarction.
It is known from post-mortem reports that fibrotic changes in the testicular tissue often occur when COVID-19 is severe. Similarly, it can be assumed that the ovaries will also be affected.

Veterinary studies have shown that the presence of viruses in the cerebrospinal fluid is correlated with the viral load in the blood of coronaviruses. The viruses are most likely to enter the nervous system in immune cells. Neurological and neuropsychiatric symptoms are not uncommon complications with COVID-19. Epileptic seizures, cognitive impairments and affect control problems can occur. The latter may be explained by a virus uptake into the nervous system via the olfactory bulb in the respiratory phase of the disease. As with any infectious sepsis, dementia as a late complication is a common complication. In principle, the SARSCoV2 virus should also be able to replicate in nerve cells, but there is as yet no reliable scientific knowledge about the extent and the possibility of rapid virus multiplication in nerve cells. Neurologic symptoms may also relate to endothelial inflammation.

There are findings that SARSCoV2 has bacteriophage properties and leads different bacteria that are commonly prevalent in the mouth, nose and throat to be more harmful. That could eventually explain why antibiotics are so essential in treatment of Covid19, as Dr Zelenko proved with Azithromycin.

Unfortunately, effective immunity rarely develops, particularly in the case of severe courses, so that in the event of a severe first systemic episode of COVID-19 that has been overcome, it must be expected that renewed infection from outside is possible.

Since the SARSCoV2 virus is taken up in erythrocytes, where it cannot replicate due to a lack of cell nucleus, a virus reservoir in the erythrocytes persists even after systemic disease phases have subsided, which can occasionally trigger auto-re-infections in the sense of relapse fever. There have also been reports of medication-mitigated disease-free pneumonia that also have malaria-like relapsing symptoms that are most likely to be mild viremia. Erythrocytes have an average survival time of approx. 100 days and are degraded by immune cells, especially in the spleen, which, with sufficient viral load, leads to renewed viremia, without a simultaneous antiviral medication, due to a high percentage of virus-infected erythrocytes with a weak immune response systemic episode of disease.

Because the progression of COVID-19 disease with systemic episodes is difficult to treat and has a poor prognosis, early drug treatment appears to be absolutely necessary in all cases that are not associated with very mild symptoms. It is not necessarily a question of complete virus eradication, since any relative reduction in virus replication also helps to reduce the course of the disease and thus reduce the risk of death and the development of late complications.

In children, severe courses with multi-organ failure and fatal outcome are less common. Since the child's immune system is not yet fully developed, SARSCoV2 is usually not as targeted in children as in adults
trigger immune-regulatory processes described above, which are of central importance for pathogenicity.

The pathogenicity is also gender-dependent, which can best be explained by the role of sex hormones in RAS with the influence of aldosterone. The RAS is more reactive under the influence of male sex hormones and so the SARSCoV2 viruses can find more docking sites, which can contribute to an average faster virus multiplication after infection in men.

The public is currently often postulating that there are no effective drugs against COVID-19 and one has to wait until a vaccine is available. The opposite is the case: there are definitely some known effective substances and medication strategies that can have a significantly positive impact on the course of the disease or even prevent infection or triggering the disease in the event of infection, even if these scientific mechanisms of action described with good evidence are still due to the time pressure could not go through the regulatory approval process.

On the other hand, there is little hope for the development of a well-effective vaccine, because even after the appearance of SARS 17 years ago, despite intensive efforts, it has not been possible to develop effective vaccines against coronaviruses for humans. The ubiquitous coronaviruses, which lead to common colds, also do not have the property of causing longer-lasting immunity in humans, which is why these infections can be acquired again and again. Developing immunity through cross-reactions is just as unlikely as building up herd immunity, which, just like the hope of a vaccine, will remain pious wishful thinking without sufficient scientifically based evidence. The pathomechanism of COVID-19 described above with the targeted immunodysregulatory effect due to the preferred

involvement of lymphocytes, analogous to the pathomechanism in AIDS, usually prevents a normal immune response, as is known from other viral infections. It would be most conceivable that a limited effectiveness of a vaccine could have a certain chance of success through the replication of thermolabile SARSCoV2 viruses, analogous to the veterinary procedure in the feline coronavirus epidemic FIP.

One must therefore assume that it will only be possible to get the epidemic under control through consistent virus isolation and drug strategies, possibly also as prophylaxis. The alternative of allowing a "controlled epidemic" of the population appears to be undesirable for all people due to the devastating effects described above, with a significant reduction in the average life expectancy by several years and a massive disruption to the general quality of life due to permanently necessary tightened hygiene measures and the associated restrictions on fundamental rights.

Conclusion

SARSCoV2 is a zoonotic virus that carries properties of typical coronaviruses and of HIV. Furthermore it seems to be a bacteriophage that reacts symbiotic with bacteria that live in the mouth, nose and throat and makes them more harmful.
There seem to be more than only one pathomechanism. The different pathomechanisms and their interactions make it very difficult to understand how exactly Covid19 deteriorates the health of infected persons and why it's pathogenecty is so different in each affected human.
The immunodysregulatory effect of the pathogen means that it is very difficult for the human body to build up a normal immune response and one cannot count on the development of individual immunity or herd immunity. The development of a well-effective vaccine is not very promising.
The course of the disease of COVID-19 can be differentiated into two phases: a respiratory phase, which can pass into a second systemic phase if there is a high initial viral load and/or a weakened immune system.
Depending on its severity, Covid-19 triggers pronounced fibrosing organ changes with serious loss of function.
Because of the great individual and social damage, the population should be prevented from being infected.
The systemic phase of the disease with viremia often shows a foudroyant course with multiple organ involvement and there is a possibility that auto-reinfections occur. Therefore COVID-19 can be described as **relapsing fever**. The erythrocytes play an important role as the most likely retreat for SARSCoV2-viruses in the body.
Well-effective drug treatment methods are available with sufficient first evidence, which should be prescribed on an outpatient basis in the early stage of the disease,

ideally contactlessly with telemedicine. This requires a easily accessible test infrastructure. Limitations on outpatient prescription options are counterproductive.