

Considering new methods for COVID-19 resisting.

Jiayi Zhang*

Department of Physical Science and Technology, Lanzhou University, Gansu, China

Abstract

COVID-19 causes great troubles to the society. Such disease is severe and acute with high mortality, leaving lesions even after it is cured. Vaccination is just a way to enhance human's immunity, and human's immunity has limitation, like human's mobility can't win that of a vehicle; therefore, vaccination is not enough to solve the problem, more creative solution is urgently in need.

Keywords: Coronavirus; COVID resisting; Evolution; Anti-virus

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Introduction

Normal influenza viruses are also coronaviruses, being inspired by the idea that the competition between normal coronaviruses and COVID-19 may restrain the replication of COVID-19, after having investigated some literatures about ecology, immunity and virology, a new ecological idea to control the COVID-19 is proposed [1]. But this is just an overall theory that needs more detailed works as well as a spur used to induce more valuable relevant researches, such as the effects of the Chinese medicines or other anti-virus foods, practices showed that Chinese medicine mysteriously have good effects on virus control.

Materials and Methods

Competition between species

Competition is an ecological concept that describes the conflicts between different species which live on same resources. For example, the rabbits and sheep would contend for the same grass in their living area [2]. When the grass is abundant, there is nothing between these two species. But once the grass becomes more and more scarce, the satiety of the sheep would be based on the hungry of the rabbits.

Competition, predation, mutualism and parasitism are four major relations between species. Competition exist not only between different species but also a same population of a species [3]. It is generally caused by the overlap in using the environment resources for their lives. Moderate competition could promote the survival of the species. Since only those stronger and more capable individual gain more live materials, the population prefers these individuals hence they become more and more sophisticated and mighty. Such process would continue as long as the environment is still habitable cause evolution. Evolution makes the population more and more suitable to live in the environments they experienced [4].

Darwin said only those who are fittest will survive, this is the natural selection principle, and this is just what makes the creatures evolve. Usually a species would generate mutation as they reproduce. With this principle, those who is fittest to the environment would propagate more while those weaker would

die out. The population as well as the individuals in it would become fitter and fitter to live in their environments [5]. Such mechanism is also what realizes herd immunity, it sacrifices those weaker individuals to make the whole group more fit to the environment. There is also another type of competition, called apparent competition. It is caused common predator of two species. When two species are predated by same predator, there is always one species avoids such predation *via* variation. As the evolution continues, one species would no longer be predated by that predator [6]. In summary, competition makes individuals in a population have to become mightier to live. Moderate competition is beneficial to the evolution of the species, although excessive competition would make the species extinct.

Immunity and equilibrium between human and microorganisms

The immunity in human being is the system that resists the outer invaders that do harm to the host. The immunity works as a whole like a symphony, and only the integration of every parts of it could constitute the complete system. Every part of it works harmonically. The immunity is what protect the host from being invaded by any factors of the environment. The immune system makes use of the recognition mechanism which involves cell-surface molecules that are able to specifically bind and adhere to other molecules on opposing cell surfaces [7]. In brief, human's immunity consists of innate immunity and adaptive immunity. The innate immunity is the part that prevent the human from infection naturally and has no specificity, such as skin, gastric acid and phagocytes etc. The feature of it is that it needs no time to response without memory, like sterilization [8].

The adaptive immunity is the part that eliminate the invader with recognition so that the factors of human themselves could be reserved while the foreign factors would be eliminated or neutralized. It needs time to respond, usually from few days to few weeks, and leaves memory for same antigen, i.e., the response to same invader would be more rapid and stronger [9]. The adaptive immunity is mainly constructed by B and T lymphocytes which have abilities to recognize particular foreign molecules and to eliminate specific molecules. They

both have different types of cell-receptors that are specific to different epitopes.

T lymphocytes play a role as a commander, they secrete cytokines that regulating many cells needed to mount an effective immune response. Such process would facilitate elimination of the antigens *via* stimulating the growth or activation of other cells including B cells which would produce antibodies to resist the invader.

B lymphocytes contain specific B-cell receptors which respond to different antigens. Once antigens bind to a B lymphocyte, those receptors would subsequently get secreted as anti-bodies following B-cell activation. They act just like soldiers, secreting antibodies that eliminate the antigens.

T cells and B cells are all stemmed from the combination of immunocompetent lymphocytes with the foreign antigens. Under appropriate conditions they proliferate and differentiate into corresponding epitope-specific lymphocytes, and this is why it needs time for immune system to respond as well as the immune system has memory [10].

In the generation of specific T cells and B cells, some lymphocytes may differentiate into self-reactive lymphocytes, but they would normally be aborted by other regulatory cells of immune system taking charge of such tasks. And the disorders of this mechanism would cause autoimmune reactions. Inflammation is also an effect in human's immune system in which monocytes and macrophages are induced to migrate to specific areas, and the disorders of the immune system could cause chronic inflammation. Inflammation is potentially harmful to human; such that improper inflammation would also hurt the body and this may also be a factor that increases the death rate in COVID-19 infection.

The adaptive immunity is also the base for vaccination. A vaccine is just some antigens that is weakened but could induce the immune responses. Injected with vaccination, the immunity was exercised so that it would have memory to that kind of antigen. When the real invaders come, the more rapid and stronger immune response would help the body to defeat the invader more successfully. Smallpox was eliminated in this way and it is the first case of vaccination. In late eighteenth century, people were killed by smallpox. But an English physician Edward Jenner found that people who were infected by cowpox but recovered would not be infected by smallpox or cowpox anymore.

In view of adaptive immunity, cowpox and smallpox contain same antigen, and the cowpox make the immunity respond to smallpox more rapid and stronger so that smallpox could be eliminated in time and people would not be threatened by smallpox anymore. This indicates that human's immunity has potential to resist the smallpox but may have no sufficient time to respond to it. And vaccination makes it prepared for that invader hence the invader would be killed before the infection is expanded. Vaccination is widely used in many infectious disease resistances today, including hepatitis B, hydrophobia and poliomyelitis etc.

Coronavirus Influenza and COVID-19 Resisting

Coronavirus is not a strange virus in our daily life. It is just those viruses that cause people to get a cold. There are many types of coronaviruses, such as Human coronavirus 229E (HCoV-229E), Human coronavirus NL63 (HCoV-NL63), Porcine epidemic diarrhea virus (PEDV), Rhinofly bat coronavirus HKU2 (Rh-BatCoV HKU2), Scotophilus bat coronavirus 512 (Sc-BatCoV 512), Miniopiteru HKU8 s bat coronavirus 1 (Mi-BatCoV 1), Miniopiteru bat coronavirus HKU8 (Mi-BatCoV) etc. Figure 1 is a photo of coronavirus under TEM, they all have an irregular shape of sphere coated with corona from children who got cold. It is certain that influenza virus and SARS virus all belong to coronavirus (Figure 1).

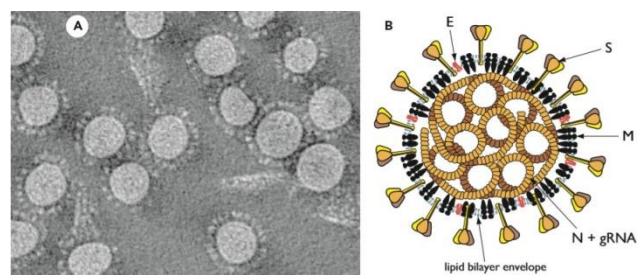


FIGURE 28.2. Coronavirus structure. A: Cryo-electron tomographic image of purified virions of mouse hepatitis virus (MHV), reconstructed as described in reference 415. (Courtesy of Benjamin Neuman, David Bhella, and Stanley Sawicki.) B: Schematic showing the major structural proteins of the coronavirus virion: S, spike protein; M, membrane protein; E, envelope protein; and N, nucleocapsid protein.

Figure 1. Coronaviruses under electronic microscope cited from fields virology.

All viruses don't have independent mechanism to reproduce themselves, they must deliver themselves into a host cell and use the resource from it to reproduce. The infection of coronaviruses all begins at binding of virions to cellular receptors. The interaction between S protein and its cognate receptor constitutes the principal determinant governing coronavirus host species range and tissue tropism. No binding, no infection. Then comes the processes of translation, transcription, replication, assembly and release so that more virions would be produced by the host, as Figure 2 from *FIELDS VIROLOGY* by David M. Knipe and Peter M. Howley. P833 (Figure 2).

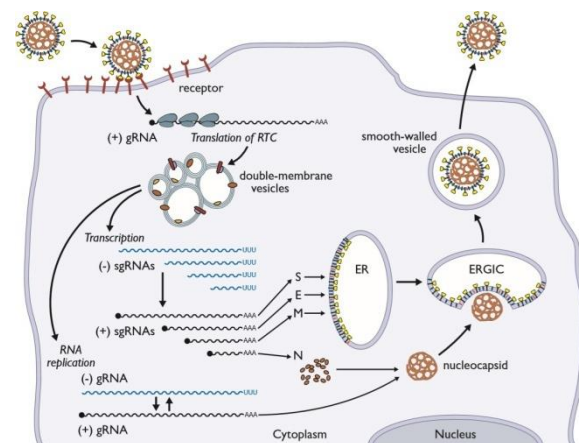


FIGURE 28.6. Overview of coronavirus replication (see text for details).

Figure 2. Coronavirus replication.

The process needs polymerase which is translated from the virus RNA, then transcribes minus RNA from the virus RNA which is used as the model for replication of the next generation of virus RNA. Then the new generation of RNA would be used as mRNA so that late protein could be translated from it. The release of coronavirus is *via* the empty vesicle in ERGIC that would merge with the cell membrane, a complete virion would be released after this step. The replication of coronavirus does not significantly differ along different coronaviruses, they all have S protein on their surface to bind to the host cell, and the organelles used afterwards are just what is used to express the RNA that the virions injected into the cell.

Compared to normal coronavirus, SARS coronavirus has many differences. The gene of SARS coronavirus is far from the evolution tree of human coronavirus and has a similarity of 64% with cow and mouse coronavirus. It has no HE protein, its gene mutations are mainly in RNA polymerase and structural protein region. In addition, some predicted unknown proteins out of the sequence data base are found in its ORF. Its morbidity mainly focuses on youth population and leads to high mortality. The infection source of SARS is mainly those infected people. No evidence for the infectivity of infected people with no symptom, only a little infectiousness of them is possible. The virions are majorly spread through droplets of human's breath, cough and sneezing etc. When one is infected, the virus would lurk for 2 to 10 days and then begin to fever higher than 38°C. The lungs of the patient appear obvious lesion, i.e., shadows on the lungs.

These features of SARS infection are similar to COVID-19, and what is worse is that COVID-19 has better infectiousness. It could be deterred that COVID-19 is a variation of SARS coronavirus which is stronger than SARS. So, the population of the highest risk should still be the youth, the virus can cause serious lesion on the whole body of the host even it is cured, and a swimming master may lose his ability once he was infected by such virus. (These 4 paragraphs refer to pp324-325 of ref.1, SARS coronavirus.) Ways to resist such virus is urgently needed.

Currently the only effective way to control SARS is quarantining, no vaccination for it. The curation for it is hard and expensive, only the combination of Chinese medicine and western medicine could cure it, but it still remains a high mortality in such treatments. Some Chinese medicines are especially effective in disease control, such as Astragalus Membranaceus, Isatis Radix, fructus forsythia and honeysuckle. The anti-virus oral liquid which is made of these medicines shows good effects on influenza control, a cold would go away within a week with a proper intake of it as well as moderate nutrition and adequate rest (Figure 3).



Figure 3. Anti-virus oral liquid.

With the introduction previously presented, the immune system could resist the invaders with stronger and more rapid response if it was exercised by same antigens before, that's how a vaccination works. And the immune specificity is mainly determined by the epitopes on the antigens, i.e., the antigens with same epitopes may be just adequate for a vaccination. And the similarity of influenza virus and COVID-19 virus may provide possibility for effective vaccinations by the influenza virus. If influenza virus could be vaccination for COVID-19, then its strong variability would also be useful to tackle with the strong variability of COVID-19 which is caused by the property of coronavirus.

However, as mentioned before, the principle of a vaccination is just to enhance human's immunity. Similar to that the speed of the fastest human's leg can't win the wheels of a car, the strongest immunity may still not be able to resist some viruses, including COVID-19. For this reason, the hope of COVID-19 resisting should not be pinned only on vaccination. People should also look for other ways, especially outer means to enhance people's immunity or to eliminate the virus specifically.

One method on such way is to use those methods to harmful creatures controlling in ecology. Since replication patterns between different coronavirus have high similarity, as the section 1 presented, different coronaviruses may come to competition when they infected same host. Including COVID-19, the replication of it may be contended by influenza virus as they need same resource in the host when reproducing themselves. The result of such competition is similar to that of any other kinds of species, all kinds of coronaviruses would be restrained by each other. So, when a host of COVID-19 is infected by influenza virus at the same time, the less harmful influenza virus may make some contribution to COVID-19 resisting, such mechanism is what is called attacking virus with virus in ancient Chinese medicine. In the viewpoint of evolution, those who are fittest would be chosen to survive. According to virologists, COVID-19 is such kind of virus that only wants to kill the host despite whether it would live; consequently, it can't avoid the destiny of extinction because the human would always evolve and survive. If people keep to quarantine from the dead or patients with serious symptom of such virus, those variation of less harm would be more likely to survive so that the virulence of it would decay. If people don't get attacked by it anymore, it could be verified that the virus is eliminated because it can't coexist with the host.

Such feature is also a disadvantage when COVID-19 competes with normal coronaviruses that trend to coexist with the host cell, because once the host is killed by the virus no more virus would be produced and those host cells infected by normal coronaviruses are also occupied so that no resource for COVID-19 replication could be provided, then COVID-19 would become less and less when the host is infected by influenza. Using other coronavirus to compete with the COVID-19 is probably a perspective way to resist COVID-19. Nature always choose those who is fittest to live, and everything in the world tend to live harmonically. For COVID-19, it's not permitting the host to live is something

rebels the harmony of everything; hence it would definitely extinct as things evolve. In this respect, using other coronaviruses which could coexist with the host to compete with it is a way to speed up such evolution to eliminate these deadly features of COVID-19, i.e., the viruses don't allow the host to live trends to die out.

Moreover, if using coronaviruses or other viruses that have a symbiosis with human to compete with the COVID-19, the living space of COVID-19 in human being would be fully occupied by them. Since these viruses coexist with the human and have better competitiveness, COVID-19 will lose their living resources and extinct, as long as there is no artificial cultivation of COVID-19. And influenza viruses are also candidates for such viruses. Traditionally thinking, any illness is not good. But influenza is such kind of disease that does little harm to human and hence exercise the immunity of human. The strong variation of coronavirus also makes influenza never extinct so that this exercise on human's immunity could continue. Rather than finding vaccination for influenza, it may be better to use influenza viruses themselves as a vaccination that have symbiosis with human.

Not only this method, there should be much more methods using multiple subjects. Such as studying Chinese medicine in modern scientific methods, there are plenty kinds of matters that have different effects on human. We have already achieved so much success in studying those matters in chemistry and Western medicine using these methods, and the matters in Chinese medicine is much more various and complex than that, it can't be imaged how tremendous achievements would be get if studying Chinese medicine in modern scientific methods. Why anti-virus is so effective to restrain the coronavirus? There may be some mechanism that disturb the replication of the virus in such medicine, not only reinforcing the immunity of human. Solving any problem should not be limited in ways that we've known; divergent thinking and creation are necessary. Any method is available as long as it could solve the problem.

Conclusion

COVID-19 is a kind of coronavirus that fiercer than SARS. Both SARS and COVID-19 are novel mutation of normal coronaviruses of normal influenza, they are not the coronaviruses that is known in any human or animal, containing gene sequences that is unknown in data base today. Such viruses are extremely harmful to human leaving lesions on human even their infections are cured. They especially prefer the cells in lungs, and the strong infectiousness of COVID-19 makes it hard to be quarantined totally.

Vaccination is a method that enhances human's immunity so that some deadly virus could be resisted by human. However, human's immunity has limitation, like the case that human's leg can't run faster than wheels on a car. For this reason, the methods to solve such problem should not be pinned down on vaccination only, any method should be considered as long as it can solve the problem.

As an example, a biological method using the competition of a beneficial coronavirus to compete with COVID-19 in this

article was brought up. Since the COVID-19 don't allow the host to live, it would kill the host despite its own life, this makes coronaviruses that coexist with human have better competitiveness than COVID-19 hence both the human and these less harmful coronavirus would win the battle against COVID-19. Influenza may be a candidate for it since normal cold does little harm to human but exercises human's immunity. Anti-virus oral liquid made of Chinese medicine also has a good effect on coronavirus control and normal influenza is easy to be resist by human with the help of it, i.e., a cold would go away in a week averagely with proper intake of it as well as adequate rest. Many Chinese medicines mysteriously have good effects on COVID-19, it may be caused by the disturbance on virus replication or other mechanisms that are different from enhancing immunity like that of vaccination. The substances in Chinese medicine are complex and various, but have mysterious effect on the control of many diseases including COVID-19 infection, using modern scientific methods to study Chinese medicine would be a highly prospective field for researching. These are just a few ideas, and any research should not be limit in finite subjects.

It is worth to mention that organic food and scientific exercising are another two essential factors to enhance people's health. Many people died from immunity disorders in COVID-19 infection, and the lack of these factors is the mainly cause of immunity disorders. Developing more scientific research on these issues, such as increasing organic food productivity and more facilitated swimming pools, would greatly enhance people's intelligence, health while reducing the illnesses. The robots that cultivates and harvest organic vegetables and fruits using artificial neuron networks is a promising way to multiply the productivity of organic foods.

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*Correspondence to

Jiayi Zhang

Department of Physical Science and Technology

Lanzhou University, Gansu, China

E-mail: zhangjiayi19@lzu.edu.cn