COVID-19: Probiotics Role in Children and Older People to Enhance Immune System

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Abstract: Coronaviruses are a large family of viruses which may cause illness in animals or humans. In humans, several coronaviruses are known to cause respiratory infections ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). The most recently discovered coronavirus causes coronavirus disease COVID-19 Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. Most people infected with the COVID-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness. The best way to prevent and slow down transmission is be well informed about the COVID-19 virus, the disease it causes and how it spreads. Protect yourself and others from infection by washing your hands or using an alcohol based rub frequently and not touching your face. This article is an idea for probiotics which help in enhancement of the immune system.

Index Terms: Corona Virus, COVID-19, nCoV-19, Quarantine and social distancing, Signs and symptoms of COVID19, nCoV-19 treatment, Prebiotics.

INTRODUCTION: The COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes, so it’s important that you also practice respiratory etiquette (for example, by coughing into a flexed elbow). At this time, there are no specific vaccines or treatments for COVID-19. However, there are many ongoing clinical trials evaluating potential treatments. WHO will continue to provide updated information as soon as clinical findings become available? Research indicates that children and adolescents are just as likely to become infected as any other age group and can spread the disease. Evidence to date suggests that children and young adults are less likely to get severe disease, but severe cases can still happen in these age groups. Children and adults should follow the same guidance on self-quarantine and self-isolation if there is a risk they have been exposed or are showing symptoms. It is particularly important that children avoid contact with older people and others who are at risk of more severe disease. Are antibiotics effective in preventing or treating COVID-19? No Antibiotics do not work against virus they only work on infections. COVID 19 is caused by a virus, so antibiotics do not work. Antibiotics should not be used as a means of prevention or treatment of COVID-19. In hospitals physicians will sometimes use antibiotics to prevent or treat secondary bacterial infections which can be a complication of COVID-19 in severely ill patients. They should only be used as directed by a physician to treat a bacterial infection.

SYMPTOMS: The most common symptoms of COVID-19 are Fever, dry cough and tiredness. Some patients may have aches and pains, nasal congestion, sore throat or diarrhea. These symptoms are usually mild and begin gradually. Some people become infected but only have very mild symptoms. Most people (about 80%) recover from the disease without needing hospital treatment. Around 1 out of every 5 people who get COVID-19 becomes seriously ill and develops difficulty breathing. Older people, and those with underlying medical problems like high blood pressure, heart and lung problems, diabetes, or cancer, are at higher risk of developing serious illness. However anyone can catch COVID-19 and become seriously ill. Even people with very mild symptoms of COVID-19 can transmit the virus. People of all ages who experience fever, cough and difficulty breathing should seek medical attention. How can we protect others and ourselves if we don’t know who is infected? Practicing hand and respiratory hygiene is important at ALL times and is the best way to protect others and yourself. When possible maintain at least a 1 metre (3 feet) distance between yourself and others. This is especially important if you are standing by someone who is coughing or sneezing. Since some infected persons may not yet be exhibiting symptoms or their symptoms may be mild, maintaining a physical distance with everyone is a good idea if you are in an area where COVID-19 is circulating.
I. Could probiotics protect against SARS-CoV-2 virus infection IN CHILDREN AND OLDER PEOPLE and aid in avoiding COVID-19?

II. Could probiotics help our immune system to prevent or potentially fight Coronavirus infections?

Key words:
Coronaviruses, SARS-CoV-2 virus and COVID-19 disease: the facts

“Corona” means “Crown” in Latin, and it refers to the distinctive shape of these viruses, where the genetic material (single stranded RNA) is contained within an envelope which has protein spikes pointing outside the structure (3). This gives a specific “crown morphology” to all Coronaviruses.

In some cases, Coronaviruses can spread from animals to humans in a process called spillover zoonosis, where many animal hosts can carry the virus before it reaches humans. When this happens, Coronaviruses can cause different types of respiratory and sometimes gastrointestinal disease. Respiratory diseases caused by Coronaviruses can range from symptoms resembling that of common colds to severe pneumonia, but for the vast majority the symptoms are mild, and people recover after few days of infection.

In December 2019, a new type of Coronavirus causing a cluster of pneumonia cases and deaths, emerged in the city of Wuhan, China, and rapidly spread-out to other countries in the world, to become today a pandemic outbreak, according to WHO. This new Coronavirus, called SARS-CoV-2 based on its genetic similarities with SARS-CoV (the virus identified in 2002 as the cause of Severe Acute Respiratory Syndrome), has been originally linked to a sea food and live animal market in Wuhan. It has been transferred to humans from a yet non-accurately identified animal. Most probably this newly discovered virus originated in bats, and since a 96% identical virus was isolated, these animals could have been intermediate hosts before the virus transferred to humans.

The new identified Coronavirus is the 7th known human Coronavirus

1) Human Coronavirus 229E (HCoV-229E)
2) Human Coronavirus OC43 (HCoV-OC43)
3) SARS-CoV
4) Human Coronavirus NL63 (HCoV-NL63 New Haven Coronavirus)
5) Human Coronavirus HKU1
6) Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
7) SARS-CoV-2

This virus is completely new for our immune system. Before the current outbreak, no humans are known to be exposed to it. Therefore, our immune systems are naive to the virus and have subsequently not had the chance to develop natural immunity against it. This is one of the reasons why the virus is spreading so rapidly through the population. Healthcare professionals are still in the process of understanding how this virus is transmitted, what is the physiopathology associated to its infection and what could be the therapeutic targets and strategies. On February 11th, WHO has named the disease caused by SARS-CoV-2 responsible for the actual global pandemic outbreak as Corona Virus Disease.

There is no specific treatment for COVID-19 yet. Treatment is focused on supportive care, providing oxygen, fluids and respiratory support for severely ill people. Early epidemiological data has shown some potential positive treatment of COVID-19 with these three drugs and potential vaccines:

Vaccine: many subcellular vaccinal strategies have been under consideration and in most of the cases a potential candidate vaccine will not be available for at least one-year.
Chloroquine: an anti-malarial drug

**Genome of the virus**

**Coronavirus genome structure and replication.**

In addition to the SARS coronavirus (treated separately elsewhere in this volume), the complete genome sequences of six species in the coronavirus genus of the coronavirus family [avian infectious bronchitis virus-Baudette strain (IBV-Baudette), bovine coronavirus-ENT strain, human coronavirus-229E strain (HCoV-229E), murine hepatitis virus-A59 strain (MHV-A59), porcine transmissible gastroenteritis-Purdue 115 strain (TGEV-Purdue 115), and porcine epidemic diarrhea virus-CV777 strain (PEDV-CV777)] have now been reported. Their lengths range from 27,317 for HCoV-229E to 31,357 for the murine hepatitis virus-A59, establishing the coronavirus genome as the largest known among RNA viruses. The basic organization of the coronavirus genome is shared with other members of the Nidovirus order (the torovirus genus, also in the family Coronaviridae, and members of the family Arteriviridae) in that the nonstructural proteins involved in proteolytic processing, genome replication, and sub genomic mRNA synthesis (transcription) (an estimated 14-16 end products for coronaviruses) are encoded within the 5'-proximal two-thirds of the genome on gene 1 and the (mostly) structural proteins are encoded within the 3'-proximal one-third of the genome (8-9 genes for coronaviruses). Genes for the major structural proteins in all coronaviruses occur in the 5' to 3' order as S, E, M, and N. The precise strategy used by coronaviruses for genome replication is not yet known, but many features have been established. This chapter focuses on some of the known features and presents some current questions regarding genome replication strategy, the cis-acting elements necessary for genome replication [as inferred from defective interfering (DI) RNA molecules], the minimum sequence requirements for autonomous replication of an RNA replicon, and the importance of gene order in genome replication.

A family of enveloped RNA viruses that are distributed widely among mammals and birds, causing principally respiratory or enteric diseases but in some cases neurologic illness or hepatitis. Individual coronaviruses usually infect their hosts in a species-specific manner, and infections can be acute or persistent. Infections are transmitted mainly via respiratory and fecal-oral routes. The most distinctive feature of this viral family is genome size: coronaviruses have the largest genomes among all RNA viruses, including those RNA viruses with segmented genomes. This expansive coding capacity seems to both provide and necessitate a wealth of gene-expression strategies, most of which are incompletely understood. Two prior reviews with the same title as this one have appeared in the Advances in Virus Research series The earlier of the two noted that the recognition of coronaviruses as a separate virus family occurred in the 1960s, in the wake of the discovery of several new human respiratory pathogens, certain of which, it was realized, appeared highly similar to the previously described avian infectious bronchitis virus (IBV) and mouse hepatitis virus (MHV) (Almeida and Tyrrell, 1967). These latter viruses had a characteristic morphology in negative-stained electron microscopy, marked by a "fringe" of surface structures described as "spikes" (Berry et al., 1964) or "club-like" projections Such structures were less densely distributed and differently shaped than those of the myxoviruses. To some, the fringe resembled the solar corona, giving rise to the name that was ultimately assigned to the group. Almost four decades later, recognition of the same characteristic virion morphology alerted the world to the emergence of another new human respiratory pathogen: the coronavirus responsible for the devastating outbreak of severe acute respiratory syndrome The sudden appearance of SARS has stimulated a burst of new research to understand the basic replication mechanisms of members of this family of viral agents, as a means toward their control and prophylaxis. Thus, the time is right to again assess the state of our collective knowledge about the molecular biology of coronaviruses.

**Taxonomy**

Coronaviruses are currently classified as one of the two genera in the family Coronaviridae However, it is likely that the coronaviruses, as well as the other genus within the Coronaviridae, the toroviruses will each be accorded the taxonomic status of family in the near future Therefore, throughout this review, the coronaviruses are referred to as a family. Both the coronaviruses and the toroviruses, in addition to two other families, the and been grouped together in the order Nidovirales. This higher level of organization recognizes a relatedness among these families that sets them apart from other non segmente positive-strand RNA viruses. The most salient features that all niodviruses have in common are: gene expression through transcription of a set of multiple
3′-nested sub genomic RNAs; expression of the replicase polyprotein via ribosomal frame shifting; unique enzymatic activities among the replicase protein products; a virion membrane envelope; and a multispanning integral membrane protein in the virion. The first of these qualities provides the name for the order, which derives from the Latin nido for nest. In contrast to their commonalities, however, nidovirus families differ from one another in distinct ways, most conspicuously in the numbers, types, and sizes of the structural proteins in their virions and in the morphologies of their nucleus.

**Probiotics and COVID-19 disease** Since there is no vaccine available or specific efficacious clinically proven treatment at the moment, preventing COVID-19 by maintaining high hygiene by washing our hands, avoiding contact with infected people and reinforcing our immune system are the best strategies. Our body, and especially our gut, is home to trillions of beneficial bacteria that live in perfect harmony, helping us to digest food, eliminating toxins, producing active molecules and educating our immune system to protect us against harmful microbes. Scientists have named this microbial ecosystem the intestinal microbiome. Today science has reached a solid level of understanding of the correlations observed between gut microbiome structure and composition and health or disease. It has been recently observed that an alteration of the physiological homeostasis of intestinal microbiota, also known as dysbiosis, is correlated with some diseases. A more detailed comparison of characteristics of these virus families has been given by. Members of the coronavirus family have been sorted into three groups which, it has been proposed, are sufficiently divergent to merit the taxonomic status of genera. Classification into groups was originally based on antigenic relationships. However, such a criterion reflects the properties of a limited subset of viral proteins, and cases have arisen where clearly related viruses in group 1 were found not to be serologically cross-reactive).

Consequently, sequence comparisons of entire viral genomes (or of as much genomic sequence as is available) have come to be the basis for group classification. Almost all group 1 and group 2 viruses have mammalian hosts, with human coronaviruses falling into each of these groups. Viruses of group 3, by contrast, have been isolated solely from avian hosts. Most of the coronaviruses in have been studied for decades, and, by the turn of the century, the scope of the family seemed to be fairly well-defined. Accordingly, it came as quite a shock, in 2003, when the causative agent of SARS was found to be a coronavirus (SARS-CoV). Equally astonishing have been the outcomes of renewed efforts, following the SARS epidemic, to detect previously unknown viruses; these investigations have led to the discovery of two more human respiratory coronaviruses, HCoV-NL63 and HCoV-HKU1. Three distinct bat coronaviruses have also been isolated: two are members of group 1, and the third, in group 2, is a likely precursor of the human SARS-CoV. In addition, new IBV-like viruses have been found that infect geese, pigeons, and ducks.

1. Schematic of the coronavirus virion, with the minimal set of structural proteins
2. The spike (S) protein. At the right is a linear map of the protein, denoting the amino-terminal S1 and the carboxy-terminal S2 portions of the molecule. The arrowhead marks the site of cleavage for those S proteins that become cleaved by cellular protease(s). The signal peptide and regions of mapped receptor-binding domains (RBDs) are shown in S1. The heptad repeat regions (HR1 and HR2), putative fusion peptide (F), transmembrane domain, and endodomain are indicated in S2. At the left is a model for the S protein trimer.

The membrane (M), envelope (E), and nucleocapsid (N) proteins. At the right are linear maps of the proteins, denoting known regions of importance, including transmembrane (tm) domains. At the left are models for the three proteins.

Coronavirus genomic organization. The layout of the MHV genome is shown as an example. All coronavirus genomes have a 5’ cap and 3’ poly (A) tail. The invariant order of the canonical genes is replicase-S-E-M-N. The replicase contains two ORFs, 1a and 1b, complete expression of which is accomplished via ribosomal frame shifting. Accessory proteins (2a, HE, 4, 5a, and I, in the case of MHV) occur at various positions among the canonical genes.
Probiotics and COVID-19 disease

Since there is no vaccine available or specific efficacious clinically proven treatment at the moment, preventing COVID-19 by maintaining high hygiene by washing our hands, avoiding contact with infected people and reinforcing our immune system are the best strategies.

Our body, and especially our gut, is home to trillions of beneficial bacteria that live in perfect harmony, helping us to digest food, eliminating toxins, producing active molecules and educating our immune system to protect us against harmful microbes. Scientists have named this microbial ecosystem the intestinal micro biome. Today science has reached a solid level of understanding of the correlations observed between gut micro biome structure and composition and health or disease.

Probiotic bacteria can interact with our gut micro biome to reinforce our immune system, increase immune responses and promote specific immune signaling with physiological relevance. During the last decades, several probiotics have shown to prevent and/or decrease the duration of either bacterial or viral infections. Most of the information available today about the reinforcement of immune health through probiotics has been demonstrated in animal models. In mice, intranasal inoculation of *L. reuteri* or *L. plantarum* have been shown protective effects against pneumonia virus lethal infection.

Nevertheless, even if some patterns are common, not all probiotics involve the same mechanisms of action. Strain specificity is crucial to define the right probiotic for the right indication. Moreover, probiotics and prebiotics have been shown to be effective in elevating immunogenicity by influencing seroconversion and seroprotection rates in adults inoculated with influenza vaccines. Combining probiotics with vitamins could also be a valid strategy to boost the immune system in a generic manner. For instance, vitamin D can modulate innate and adaptive immune responses beyond its effects on bone and calcium homeostasis. Indeed, it has been demonstrated that not only vitamin D receptor is expressed on immune cells surface but also that all immunologic cells are able to synthesize vitamin D metabolite.

Health starts in the gut

80% of our immune defense is located in our gut and a balanced micro biota and enough of good bacteria are important for a well-functioning immune system. The good bacteria educate the immune system, making it ready to fight unwelcome invaders like bad bacteria and toxins. To achieve a healthy balance the good bacteria need to outnumber the bad with ten to one.

If bad bacteria for some reason start to exceed it may lead to an imbalance in the digestive system, called dysbiosis. Dysbiosis may cause problems like diarrhea, constipation, bloating, temporary stomach pain and leaky gut. Also, new research indicates that there probably is a strong connection between an unbalanced micro biota.
Problems today

The fact that our lifestyle has changed dramatically over the last 50 years has definitely left its marks. Modern ways of living with increased urbanization and altered eating habits have resulted in an imbalance of our micro biota.

Our micro biota is negatively affected by the following

- Usage of antibiotics and other drugs – antibiotics do not only kill pathogens, they also kill our good bacteria
- Obsessive hygiene – showering several times a day, using germ killing soap and detergents are depleting our micro biota
- Birth by Caesarean section – babies born by C-section don’t pass through the birth canal and are therefore not exposed to the desirable variety of good bacteria from their mother
- Poor eating habits – fast food, processed food, coffee and alcohol. It may taste good, but unfortunately your gut bacteria do not thrive on junk food, they need fibers, fresh fruits and vegetables
- Stressful living and lack of sleep – both stress and too few hours in bed may lead to changes in composition and reduction of microbial diversity
- Excessive exercising – while your workout at the gym is beneficial for your general well-being, professional athletes are often exercising at a level that harms their micro biota and puts their immune system under stress, making them more susceptible to infections.

Gatekeepers in the gut

The epithelial lining covers our gastrointestinal tract and works like a skin on the inside. The main task is to differentiate between what should be absorbed and what should not be let into our bodies. To its help it has gatekeepers, so called tight junctions. Their function is to let certain things like nutrients, vitamins and water through, and prevent things like toxins and pathogens, from passing through from your digestive system into your body and your bloodstream.

While a well-balanced micro biota makes the epithelial lining stronger, tighter and better performing, an imbalance in the gut damages the epithelial cells. Leaky gut is a condition caused by a damaged epithelial lining. The gatekeepers, the tight junctions, are letting things through that should normally not enter into the bloodstream. This may lead to several conditions and health problems, for example sepsis, inflammation, allergies and intolerances and digestive problems like IBS.
**Good bacteria**

Good bacteria can be found in food. Long before refrigerators and freezers, people used bacteria in fermentation to prolong the shelf-life of food. Examples of fermented foods are yoghurt, sauerkraut, and pickled vegetables. Common lactic acid bacteria used for fermentation are *Lactobacillus acidophilus*, *Lactobacillus bulgaricus* and *Streptococcus thermophiles*.

Truly healthy bacteria are known as probiotics. Probiotics are live bacteria that are proven to benefit our health by restoring the bacteria balance in the body and thereby have a positive effect on several health conditions. They are usually consumed as food supplements. Examples of common probiotic strains are *Lactobacillus reuteri* Protectis, *Lactobacillus rhamnosus* GG and *Bifidobacterium animalis* ssp.

**Bad bacteria**

A small percentage of all bacteria on earth are pathogenic, meaning they may cause health problems and disease. Food poisoning may be caused by *E. coli* and *Salmonella*, sepsis by *S. aureus* and *S. pneumoniae* can give pneumonia.

It is important to remember that bacteria of the same species but of different strains can behave completely different. Some species, like *E. coli*, harbor strains that are extremely pathogenic, like EHEC and ETEC, causing severe diarrhea. On the other hand, some strains of *E. coli* are commensals and they are one of the most common bacteria we carry in our gastrointestinal tract.
Where do our probiotic strains come from?

Today probiotic bacteria are produced in modern production facilities under controlled conditions to ensure that the product you buy contains exactly the same bacterial strain every time. The bacteria are cultured with the correct food and temperature to grow and duplicate. Through careful testing and quality control, each dose has the right number of viable organisms with no contaminants.

Conclusions:

There is no scientific rationale of using probiotics to protect, prevent or treat COVID-19 and SARS-CoV-2 infection specifically.

Nevertheless, we strongly support the reinforcement of our immune system by any scientifically valid strategy. Help in maintaining a healthy gut microbial diversity and prevent, intestinal dysbiosis in elderly, infants and the general population is important.

Combining a healthy and balanced diet together with prebiotics, probiotics, vitamin supplementation, among others, could help us to reinforce our immune system during the COVID-19 outbreak.

Microorganisms and humans have coexisted since the dawn of the time. Over the eons, microorganism and humans have indeed been an integral aspect of the nature. Humans have been employing microorganisms for research which has in turn provided answers to many human queries from the context of health and well-being. Microorganisms are not of research prominence but are an integral part of human system which comprises of fulltime and part time pathogens. Though the novel disease causing agent is often compared to some of its members that are known to cause similar kind of clinical manifestation, it is regarded as novel because of its ability to rapidly spread among people which differentiates it from its earlier contenders. The virus that is commonly called a COVID-19 is a pleomorphic, mutating virus and is known for contact spreading. Though the disease started as an epidemic in the Wuhan province of China, it soon spread all over the world resulting in a pandemic condition. Young children and older adults are highly susceptible to the disease which targets the respiratory system. The initial symptoms of the disease causes cold like signs associated with fever and cough which in later stages transforms in severe acute respiratory syndrome causing severe respiratory manifestation and under further stages can lead to death because of multiple organ failure.

Several organizations have attempted to curb the incidence of the disease by creating awareness. Legal bodies and authorized firms have undertaken appropriate measures to safeguard the people. Extensive screening at various entry and exit points were carried out for the isolation of patients with positive COVID-19 symptoms and the isolated patients were sent to quarantine centers installed at different places.

Recent studies also validate the spread of the disease by person to person contact. If we enhance our immune system we are safe from the damage of the virus.

Probiotics are playing important role to improve our immune system. There is no effective vaccine or medicine for the contagion but some studies reveal the usefulness of chloroquin and sodium hypochlorite (as a disinfectant for cleaning the objects and floor). However, according to WHO, vaccine is yet to be discovered and quarantine measures like self-isolation and social distancing are currently followed to reduce the community infection.
It could be rightly said that staying at homes is not only for our safety but is to safeguard others from getting the infection. This article only attempt to provide a drop of information about the contagion and further research is necessary to comprehend COVID-19.

References


(8)WHOsource: https://www.who.int/emergencies/diseases/novel-coronavirus2019/events-as-they-happen
