

Could a healthy microbiome reduce COVID-19 symptoms?

The SARS-CoV-2 virus causing the COVID-19 pandemic is an ongoing global health crisis. Symptoms of infection can range from very mild to fatal, but the determinants of severity are still under research. Dr Lubomír Janda at the Veterinary Research Institute, Czech Republic, and his colleagues suggest that the microbiome could be a factor influencing the severity of COVID-19 symptoms. In particular, they suggest that a healthy intestinal microbiome could reduce the severity of symptoms, and that the popularity of fermented foods of some central European countries such as the Czech Republic could account for the relatively low COVID-19 fatality rate in this area.

Coronaviruses (CoV) are a family of viruses capable of infecting humans and other animals. Many of the common members of the coronavirus family cause mild upper respiratory tract infections and are responsible for almost a third of colds in adults. These can also cause more

severe conditions such as pneumonia and bronchitis, but generally only in at-risk patients such as infants, the elderly, and the immuno-compromised. However, some members of the coronavirus family cause more severe disease, including SARS-CoV (severe acute respiratory syndrome), MERS-CoV

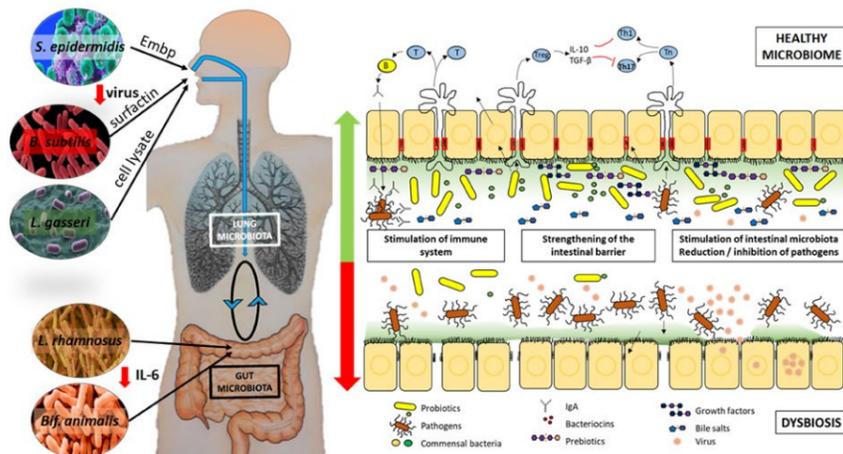


Fig 1. Graphic highlighting the role of the healthy microbiome. A healthy intestinal microbiota maintains a sufficient level of response between host immunity and pathogens. The healthy microbiome also plays a key role in the prevention of the overgrowth of pathogenic bacteria and maintenance of intestinal barrier integrity.

(Middle East respiratory syndrome) and SARS-CoV-2 (also known as COVID-19, the 2019 novel coronavirus).

Dr Lubomír Janda at the Veterinary Research Institute, Czech Republic, and his colleagues at Masaryk University and University Hospital Brno, suggest that an individual's microbiome could affect the severity of COVID-19 infection.

EFFECTS OF COVID-19

Approximately two thirds of people infected with SARS-CoV2, the virus causing COVID-19, are asymptomatic or have mild symptoms; however, severe cases can be fatal. Some of the common symptoms of COVID-19 include fever, fatigue, loss of the sense of smell or taste, and coughing or shortness of breath. Gastrointestinal symptoms such as diarrhoea and nausea can also occur, and one fifth of patients requiring hospitalisation develop cardiovascular complications which are strongly associated with risk of mortality. There is also some evidence of SARS-CoV-2 causing dermatological problems, and kidney and liver function impairments. The most common cause of mortality in COVID-19 patients is the development of acute respiratory distress syndrome (ARDS).

IMMUNE RESPONSE TO COVID-19

ARDS develops in the late stages of the disease and means that the lungs are unable to provide the body with enough oxygen. Patients who are elderly, obese, or have an underlying health condition are at the highest risk

of developing ARDS. An important characteristic of ARDS is the high levels of inflammation caused by the patient's immune system. This leads to lung fibrosis, where the lungs are damaged, and the tissue becomes thicker with scarring. This makes it increasingly difficult to breathe, leading to respiratory distress.

There is evidence suggesting that some patients with severe COVID-19 symptoms may have a hyperinflammatory syndrome resulting in sudden and fatal hypercytokinemia, also known as a cytokine storm. Cytokines are small pro-inflammatory signalling molecules released by many tissues to regulate immune response. A cytokine storm occurs when there's a positive feedback loop between cytokines and immune cells, causing an uncontrolled and excessive release of cytokine molecules. Hypercytokinemia causes the severe symptoms of ARDS and can lead to multi-organ failure. It has therefore been suggested that this hyperinflammation might be the cause of death in COVID-19.

MICROBIOME AND IMMUNE RESPONSE

The microbiome is the community of microorganisms – including bacteria, viruses and more – found in all areas of the human body. During the long course of coevolution, the communication networks between prokaryotic and eukaryotic cells have evolved to enable effective coexistence. Many different molecules, including proteins, small messenger molecules or cellular components, can be sensed and can trigger specific responses. One of them, known as the non-coding RNAs, are shared by both eukaryotic (eg. humans) and prokaryotic (eg. bacteria) cells. Microbiota, including pathogens, use the communication network to alter the host environment for their benefit by affecting metabolism, the endocrine system, the immune response and so on. The same means of communication but in the opposite direction can be used to make the tissue environment less hospitable for pathogens. There is some evidence to suggest that SARS-CoV-2 replication can be limited by the human body's non-coding RNA. The

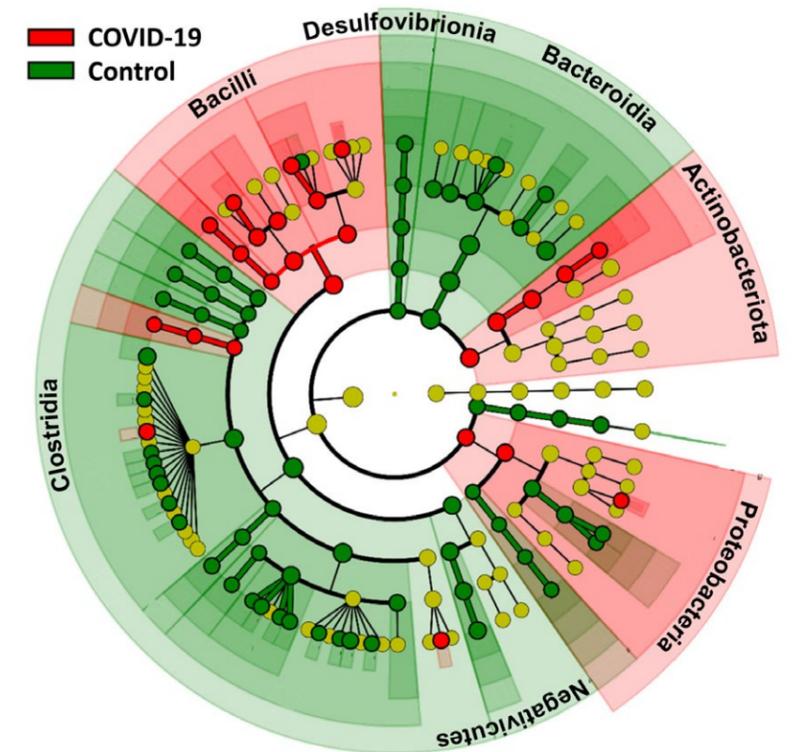


Fig 2. Visualisation of the cladogram of bacteria from Phylum (outer circle), Class, Order, Family to Genus and Species (inner circle). Related bacteria occurring only in patients with COVID-19 (red dot), only in healthy volunteers (green dot), or in both groups (yellow dot).

mediatory effect of symbiotic bacteria supports this effect. In addition, the association of chronic diseases such as diabetes, heart conditions, obesity, and allergy have been shown to correlate

influence the severity of symptoms caused by SARS-CoV-2 infection. It appears that hypercytokinemia could be highly influential in fatal outcomes associated with COVID-19 and that

Diseases such as Type 2 diabetes and cardiovascular disease, and conditions such as old-age and obesity, are associated with a change in the microbiota.

with adverse changes in microbiome composition. On the other hand, supplementation with probiotics might directly alter the proinflammatory cytokines, improve lung function, and decrease the infection burden.

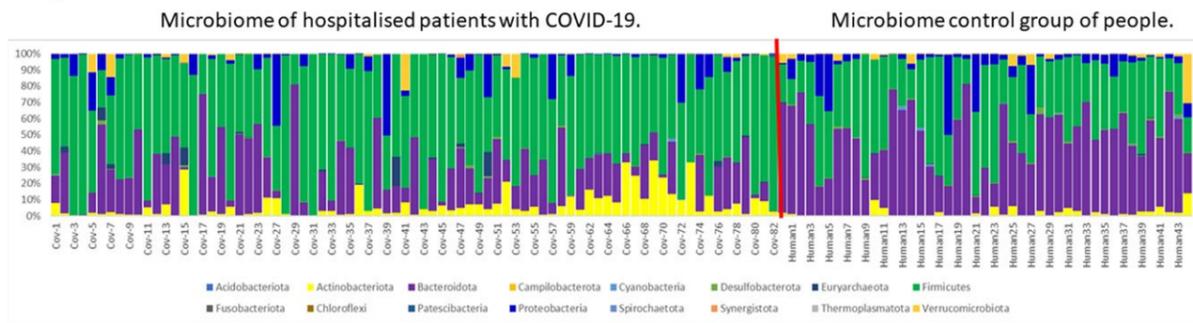
There is also evidence that some species of microbiota can directly alter immune response, with one study showing a significantly reduced pro-inflammatory cytokine presence in response to vaccination in infants given probiotics. Dr Janda and his colleagues, therefore, suggest that a healthy gut microbiome could

gut microbiota can provide a defence against pathogens and regulate the immune response.

COVID-19 AND THE INTESTINAL MICROBIOME

Viral tropism refers to the ability of a virus to infect a particular cell or tissue. SARS-CoV2 attaches to angiotensin-converting enzyme 2 (ACE2) molecules on the surface of tissues. As ACE2 is present in both lung tissue and the epithelium of the intestine, this means that the tropism of SARS-CoV2 affects both the lung and the gut. However, despite ACE2 being available at higher

Phylum



Order

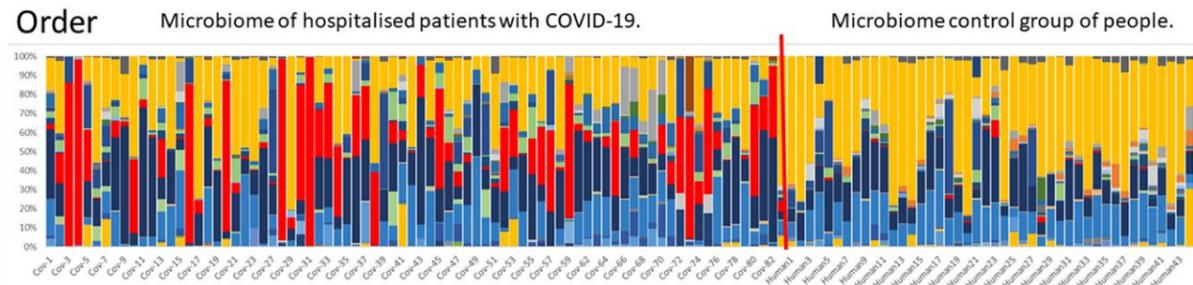


Fig 3. Microbiome of healthy volunteers compared to patients with COVID-19. Graphical representation at the level of bacterial classification 'Phylum' and 'Order'.

levels in the intestine, gastrointestinal symptoms of COVID-19 are not universal and tend to be mild. This could suggest that the gut microbiota provide some defence against SARS-CoV-2 infection.

Individuals who are elderly, obese, or who suffer from underlying chronic health conditions such as respiratory disorders, cardiovascular disease, or diabetes, are most at risk of developing severe to fatal symptoms of COVID-19. Each of these factors is also associated with a change in the intestinal microbiota, known as dysbiosis

(a reduction in the diversity of microorganisms making up the microbiome). It is not known

whether a disease causes a change in the microbiome or if a change in the microbiome allows the disease to develop, but there is a negative change in the microbiota composition associated with each of these factors. So, it is possible that, as mentioned previously, a positive change such as probiotic supplements could work against disease.

Dr Janda and his colleagues believe that supplements or alterations in

diet to improve microbiome health could function as an adjuvant therapy (helpful or facilitatory treatment intended to work alongside primary treatments) for COVID-19.

DYSBIOSIS AND POSTBIOTICS

Dysbiosis can be caused by many factors, including disease, overuse of antibiotics, or essential bacteria not being encountered or missing from the diet. However, in areas of central Europe, including the Czech Republic, some traditional foods are

In areas of central Europe including the Czech Republic, some traditional foods are high in beneficial postbiotics.

high in beneficial postbiotics. Not probiotic organisms themselves, but the products of these organisms are responsible for the positive effect on the host. Products of probiotic bacteria have the effect of reducing the severity of gastrointestinal problems and allergic conditions and support a healthy immune response. Traditional rye-wheat sourdough bread, sauerkraut, and yoghurt or other sour dairy products are common

dietary staples in the Czech Republic and are very high in postbiotics. The World Gastroenterological Organisation recommends a daily probiotic intake of at least 20 billion bacteria, but only one slice of sourdough bread (100g) alone contains the products (postbiotics) of over 100 billion bacteria present in the dough.

There is currently no direct evidence that the regular intake of postbiotics is responsible for the lower case-fatality ratio from COVID-19, but Dr Janda and his colleagues believe that this hypothesis should be investigated further. They point out that

the Czech Republic also has a lower incidence of coeliac disease than the global average, and this is an autoimmune disease known to be dependent on the health of the intestine. It is therefore possible that the widespread consumption of foods high in postbiotics in the Czech Republic helps to promote microbiome health and reduce the risk of severe symptoms resulting from SARS CoV2 infection.



Behind the Research

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Research Objectives

The use of enzymes in the treatment of resistant bacteria, probiotics as an alternative to a gluten-free diet, and the study and prevention of COVID-19.

Detail

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Bio

Lubomír Janda studied molecular biology and genetics at Charles University in Prague, receiving his PhD from the Institute of Microbiology at the Czech Academy of Sciences in 1997. He was an assistant professor at Max Perutz Laboratories at the University of Vienna until 2007 when he joined Masaryk University and later

CEITEC (Central European Institute of Technology) as an independent researcher. Since 2017, he has worked at the Veterinary Research Institute. He is a member of the Czech Microbiome Society.

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Collaborators

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- Dr Ryšávk, with whom Dr Janda collaborates, is CEO of MediPharma vision: medipharmavision.cz/cs/vyzkum

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Personal Response

In your opinion, would it be a good idea for more people to consider probiotic supplements or include more foods high in postbiotics in their diet?

Both questions can be answered yes. I was surprised at how many people around me started taking probiotics regularly during the pandemic or started baking rye-wheat sourdough bread at home. In addition to preventing COVID-19 disease, they have seen improved health. Some had improved skin, others got rid of chronic intestinal problems, my children did not have antibiotics for two years and the number of respiratory diseases decreased significantly. I just want to point out that the dose is important, because not every probiotic has 20 billion probiotic bacteria in one capsule, and not every probiotic can suit the person in question. It's good to find 'your' probiotics.

