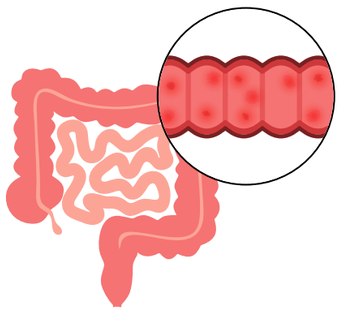
Does COVID-19 vaccination protect patients with inflammatory bowel disease?

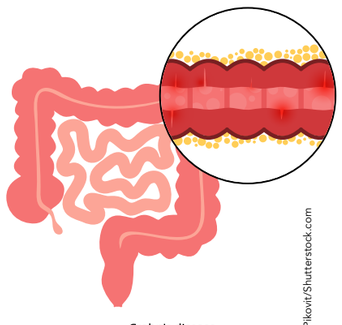
Inflammatory bowel disease (IBD) is the collective name for disorders causing chronic inflammation of the intestines, such as Chrohn's disease and ulcerative colitis. Patients with IBD typically undergo therapy using immunomodulators and corticosteroids which have a considerable impact on the immune system. Particular groups of IBD patients are therefore at greater risk of being hospitalised by COVID-19 – or even dying. Tackling these severe consequences, Professor Milan Lukáš, Dr Karin Cerna and their team at the Charles University in Prague, Czech Republic, researched whether vaccination against SARS-CoV-2 works efficiently in IBD patients, with the aim of creating a plan of action tailored to their needs during the pandemic.

The global pandemic of COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is still ongoing and continues to affect the health and lives of millions of people around the world. The development and roll-out of COVID-19 vaccines changed the course of the outbreak by dramatically reducing hospital admissions and mortality rates. Vaccination against SARS-CoV-2 has proven to be a reliable way to build protection against and immunity to the disease in people who have certain medical conditions, or who are taking medications that weaken their immune system and so are at increased risk of experiencing severe illness and dying.

In this category, patients suffering from inflammatory bowel disease (IBD) might be treated with immune-suppressing medications, causing their immune response to COVID-19 vaccinations to be weaker than in people who have healthier immune systems. There is therefore a need to test the efficacy and safety of SARS-CoV-2 vaccines for IBD patients, especially for the subset on immune-modifying treatments.



Ulcerative colitis



Crohn's disease

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Knowledge of these vaccinations' ability to provoke an immune response against COVID-19 is limited for patients with IBD. Professor Milan Lukáš, Dr Karen Cerna, and their team at Charles University in Prague have been investigating the parameters and researching the facts to ensure the safety and efficacy of the vaccines. This research aims to create helpful vaccination guidelines and antibody testing protocols for patients with IBD.

COVID-19: IBD RISK FACTOR

IBD describes long-term bowel diseases that are characterised by inflammation of the small and/or large bowel. IBDs usually fall into one of two main disease categories: Crohn's disease (which can affect any part of the gastrointestinal tract but most often the ileo-colonic region) and ulcerative colitis (which only affects the large bowel, consisting of the colon and rectum). IBD patients are more susceptible to infections such as COVID-19 – not only because of ongoing bowel inflammation but also because of the immune system-suppressing medication often used to treat the disease. Both of these factors affect the normal function of their immune system and are suspected to inhibit the production of antibodies against SARS-CoV-2.

IBD AFFECTS ANTIBODY LEVELS

Lukáš and his team set out to find out if IBD did increase a patient's risk from COVID-19. To do this, they needed to look at the rate and magnitude of seroconversion (signs that the immune system is responding to a virus), and assess the effect of immune-modifying treatments on anti-SARS-CoV-2 antibody levels.

IBD patients taking immunomodulators might be at increased risk of being hospitalised for COVID-19.

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Lukáš's research aims to create helpful vaccination guidelines and antibody testing protocols for patients with IBD.

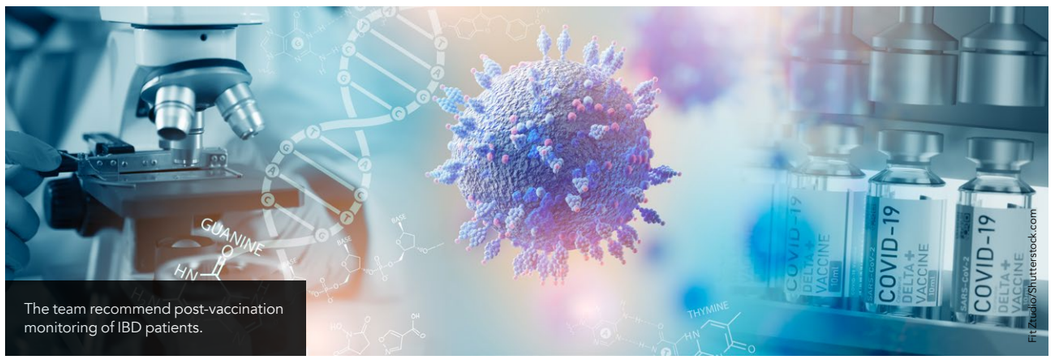
The team tested IBD patients' antibody levels by conducting a study that included 602 IBD patients and 168 healthcare workers with an intact immune system serving as controls. All the participants were vaccinated against SARS-CoV-2, either with a m-RNA vaccine (Pfizer–BioNTech or Moderna) or with the modified chimpanzee adenovirus vector vaccine (AstraZeneca). Lukáš tested the participants' antibody levels just before the vaccination and eight weeks after.

Approximately half of the IBD patients in the study were being treated with tumour necrosis factor alpha (TNF-alpha) inhibitors – a class of medicines that block the pro-inflammatory cytokine TNF-alpha to ameliorate the inflammatory process and its symptoms. Just under half of the remaining patients were receiving other medications, including other biological treatments (drugs that are manufactured in living sources and are often large, complex molecules such as proteins) and immunosuppressants like azathioprine, 6-merkaptopurine or methotrexate (a medicine that works by suppressing the function of the immune system).

The researchers discovered that 97.8% of the IBD patients and 100% of the control population had antibodies against SARS-CoV-2's spike protein post-vaccination (viral spike proteins enable viruses to enter and infect host cells). The results also revealed that these antibody levels were lower in IBD patients who were administered the modified chimpanzee adenovirus vaccine (AstraZeneca) than in those who received the m-RNA vaccines (Pfizer–BioNTech and Moderna). No evidence was found for an adverse effect of biological treatments on COVID-19 antibody levels. By analysing their data, Lukáš and his team also found that IBD patients treated with a combination regimen of TNF-alpha inhibitors and methotrexate or thiopurines (immunosuppressive drugs) demonstrated lower levels of antibodies compared to the rest of IBD patients, regardless of treatment. This finding suggests a synergistic action between the two types of medication; the combination of medication causes a greater effect than would be expected from the sum of each individually. This essentially further suppresses the immune system and eventually affects its ability to produce antibodies to protect these patients against the virus.

CELL IMMUNITY INHIBITED

The team did not stop at measuring antibody levels. Recent studies had reported that the cell immune response (the body's natural response to invading pathogens) is a more sensitive indicator of the efficacy of COVID-19 vaccinations. So besides testing the ability of IBD



The team recommend post-vaccination monitoring of IBD patients.

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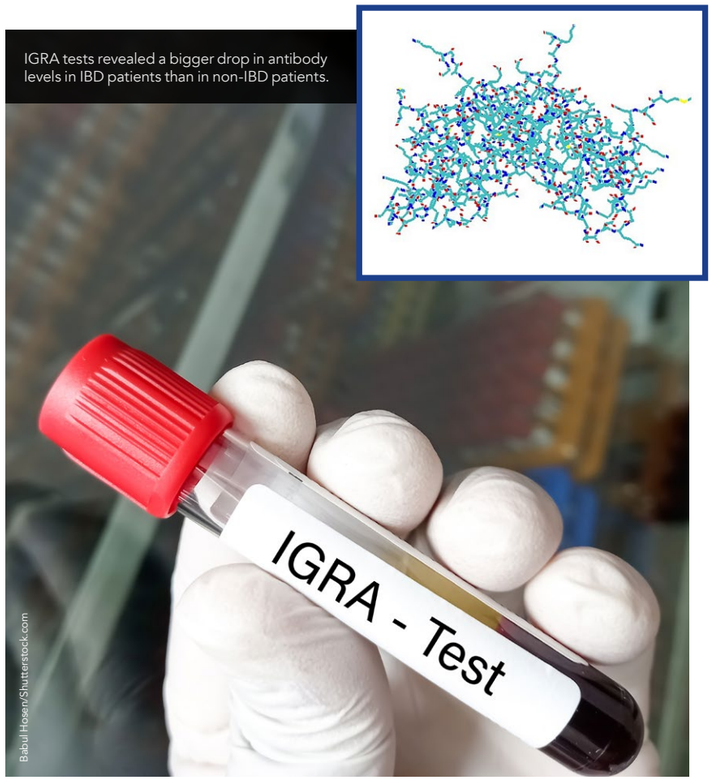

IGRA tests revealed a bigger drop in antibody levels in IBD patients than in non-IBD patients.

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patients' immune systems to produce antibodies, in their next study Lukáš and his team also investigated the efficacy of the cellular defence against SARS-CoV-2. In order to achieve this, the researchers tested the blood of 60 IBD patients and 30 healthy controls after they had been vaccinated against SARS-CoV-2. The blood was analysed for antibodies at baseline and also at eight and 26 weeks after the second vaccination, using a technique called chemiluminescent microparticle immunoassay. At week 26, the team tested for antibodies against another structural protein of the virus (anti-nucleocapsid antibodies) and interferon-gamma levels (produced by our immune cells in response to viruses) in response to viral antigens' stimulation. This was performed by using a special test called interferon-gamma (IFN-γ) release assay (IGRA).

The results of these tests revealed a significantly bigger drop in antibody levels at 26 weeks against the virus's spike protein among IBD patients compared to non-IBD patients, while the anti-nucleocapsid antibodies were not detected at all in either group; this fact indicated with a sufficient degree of probability that the vaccinees were not infected with the SARS-CoV-2 virus.

Researchers think m-RNA vaccinations, like Pfizer–BioNTech and Moderna, are the most effective for IBD patients.

Similarly, the interferon-gamma levels revealed by the IGRAs were lower in the IBD group compared to the control group, a finding that suggests that the ability of these patients' immune cells to produce interferon was impaired – especially in those under treatment with TNF-alpha inhibitors. Lukáš and his team also found that these results correlated to the respectively poor production of both types of tested antibodies in the same patients, something that confirmed their initial hypothesis.

M-RNA VACCINE MOST EFFECTIVE

Lukáš's and Cerna's research confirms that vaccination against SARS-CoV-2 is still the best strategy we have for protecting IBD patients from COVID-19. This is because the researchers found that there is an immediate and rigorous post-vaccination antibody production in most IBD patients, including those on immune-modifying treatments. The only exception was found to be the patients that were on both alpha-TNF inhibitors and immunomodulators at the same time; therefore, the team believes that extra attention should be given to these patients, initially in the form of booster vaccinations. Due to the increased antibodies produced by m-RNA vaccines like Pfizer–BioNTech and Moderna compared to the AstraZeneca vaccine, the researchers think m-RNA vaccinations are the most effective for IBD patients and should be the preferred choice when available. Since there were no safety issues identified, they also confirm that IBD patients can continue their immune-modifying therapy, even during the vaccination period. Importantly, when evaluating the laboratory activity of IBD by C-reactive protein (protein found in blood plasma which rises in response to inflammation) and faecal calprotectin (released in response to inflammation in the intestines) levels, the researchers found no significant differences before the vaccination and 26 weeks after it.

The results of the study also indicate the important role of cell immunity, especially since IBD patients undergoing immune-modifying therapy likely have a lower risk of developing COVID-19 disease if they have positive post-vaccination cellular immunity against the virus. Lukáš recommends post-vaccination monitoring of patients with IBD so that booster vaccinations can be scheduled for when the tests indicate they are required. The sample of patients tested in the study will need to be repeated using a larger population to confirm these initial findings. However, the team have made significant progress when it comes to identifying the vaccinations that give IBD patients the best protection against COVID-19.

Behind the Research

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Research Objectives

Professor Milan Lukáš and his team research the effects of COVID-19 vaccinations in inflammatory bowel disease patients.

Detail

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Bio

Professor Milan Lukáš is the author of over 250 publications in international medical journals, Editor-in-Chief of *Gastroenterologie a hepatologie*, and former President of the Czech Gastroenterological Society. He's a member of the American Gastroenterological Association, European Crohn's and Colitis Association, and International Organization for the Study of Inflammatory Bowel Disease.

Funding
IBD-COMFORT Foundation

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Personal Response

What type of future studies are needed to further evaluate the longevity of humoral (production of antibodies) and cell immune response following vaccination against SARS-CoV-2?

" Long-term follow-up of humoral and cell immune response are absolutely needed. Vaccination against SARS-CoV-2 has to be implemented within the care armamentarium in IBD patients, as with vaccination against pneumococcus or influenza. The remaining question is how often the vaccination against SARS-CoV-2 is optimally needed in the IBD population (yearly, biannually, etc). The answer is based on the long-term monitoring of humoral or cellular response after the completed vaccination. We recently learned that biologic therapy itself (anti-TNF, vedolizumab or ustekinumab) is not associated with negative impact on the results of vaccination; only when combined with immunosuppressants is there a risk. "