Study identifies cause of rapid loss of vaccination protection in autoimmune diseases

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People who are treated with TNF-α inhibitors for their autoimmune disease such as Crohn's disease or rheumatoid arthritis lose their vaccination protection significantly earlier than average. The mechanism underlying the early decrease in antibody levels has now been elucidated

by a scientific team from MedUni Vienna.

In view of the results, principal investigator Ursula Wiedermann-Schmidt emphasizes the importance of regular boosters for those affected. The research work has just been published in the journal *eBioMedicine*.

The study was conducted by the Center for Pathophysiology, Infectiology and Immunology in cooperation with the Department of Gastroenterology and Hepatology of the University Department of Internal Medicine III. Patients with inflammatory bowel diseases (IBD) such as Crohn's disease or ulcerative colitis and healthy controls were administered a SARS-CoV-2 mRNA vaccination and a booster after six months.

Subsequent analyses showed that people receiving TNF-α blocker therapy had significantly lower antibody levels than healthy subjects and IBD patients receiving another form of treatment (α4β7-integrin antagonists).

TNF-α blockers are anti-inflammatory and immunosuppressive drugs from the group of biologics that are not only used for inflammatory bowel diseases, but also for other autoimmune diseases such as rheumatoid arthritis or psoriatic arthritis.

According to the research team, the significantly faster loss of vaccine protection observed in the study is due to the fact that the strong inflammatory situation in these patients—despite the use of TNF-α inhibitors—inhibits the production of memory B cells in the lymph nodes. These are the cells of the immune system that are responsible for the production of long-lived plasma cells as well as antibodies and thus for long-term vaccine protection against already known pathogens—an essential prerequisite for the quality and duration of the protective effect

of vaccinations.

Check of vaccination status with diagnosis of disease

"In our study we were able to elucidate the exact mechanism why only short-lived plasma cells are formed under TNF-α blocker therapy, so that antibody protection only lasts for a short time," says corresponding author Wiedermann-Schmidt, Head of the Center for Pathophysiology, Infectiology and Immunology and the Outpatient Clinic for Vaccinations, Travel and Tropical Medicine at MedUni Vienna. The study results apply not only to SARS-CoV-2 vaccinations, but in principle to all vaccinations.

"For this group of patients, it is therefore necessary to maintain short-term protection through repeated booster vaccinations," says Wiedermann-Schmidt. Special attention must be paid to vaccinations that are administered for the first time under TNF-α blocker therapy—here the early antibody waning and loss of protection can be most pronounced.

Vaccinations performed already before the start of TNF-α blocker therapy would most likely retain their protective effect. In principle, when diagnosing an autoimmune disease (and other diseases under immunosuppressive therapy), the entire vaccination status should be ascertained as soon as possible and missing vaccinations should be supplemented before starting TNF-α blocker therapy (as well as other immunosuppressive therapies).

More information: Erika Garner-Spitzer et al, Lower magnitude and faster waning of antibody responses to SARS-CoV-2 vaccination in anti-TNF-α-treated IBD patients are linked to lack of activation and expansion of cTfh1 cells and impaired B memory cell formation, *eBioMedicine* (2023). DOI: 10.1016/j.ebiom.2023.104788

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