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Immune through the pandemic

>> Modern immunology is a relatively young science. Antibodies were only discovered in 1890. There is a world of difference between the scientific understanding of the Spanish flu and Covid-19. This makes it all the more astonishing how 'immunological' misunderstandings in public opinion and among political decision-makers contributed significantly to misjudgements and restrictions during the Covid-19 pandemic. Without wanting to shed light on the sociological background to this development here, it may be helpful for dealing with future pandemic challenges to name a few key misconceptions:

#1: Neutralising antibodies in the blood are not a protective correlate.

For viruses that attack us via the respiratory tract, the first problem is to penetrate the mucus of the respiratory tract. Here, in the mucus of the respiratory tract, 'neutralising' antibodies can prevent infection if they bind to the receptor of SARS-CoV-2 in such a way that binding to our cells is prevented. For some 'experts' and many others, 'neutralising', 'sterile' immunity, i.e. protection against infection as such, was the only relevant immunity. There are countless scientific publications on 'neutralising' antibodies. There was talk of 'immune escape' when a new variant of the virus was no longer 'neutralised'. Unfortunately, neutralising antibodies from the blood were examined. Very few scientists have investigated antibodies in the respiratory tract. They found that the antibodies there disappear within weeks and months after a vaccination, but also after surviving infections, even if they are still easily detectable in the blood. The problem of 'sterile' immunity is therefore the transport of antibodies from the blood to the surface of the airways. How the transport mechanisms are activated is not well understood. It would be the key to effective vaccine adjuvants that provide long-term protection against infection. Perhaps we can learn from our microbial neighbours, the bacteria of the microbiome. The bacterium Streptococcus salivarius, for example, ensures that the neutralising antibodies remain on the mucous membranes (1).

Clearly, our immune system is not designed to protect us from infection in the long term, but to protect infected individuals from serious illness and death. Neutralising antibodies in the blood are not so important for this 'systemic' immunity. It is sufficient if antibodies clump the viruses together and mark them for immune cells. It is not for nothing that nature has equipped every antibody with at least two identical binding sites for the antigen: a prerequisite for clumping, which prevents individual viruses from infecting new cells. So:

#2: Non-neutralising antibodies against SARS-CoV-2 are important for systemic immunity, protection against severe disease.

#3: Quality over quantity of antibodies.

Do we lose our immunity when the antibodies in our blood decrease? We knew better before the pandemic (2). In fact, it is not so much the quantity of antibodies that determines our immunity, but their quality. During an immune response, cells that process the viral antigen interact with the T and B lymphocytes of the immune system. B lymphocytes are activated when their antibodies bind to antigen. During a (successful) immune reaction, the antigen becomes less and less, and in the end only the B lymphocytes whose antibodies recognise the smallest amounts of antigen are activated. During this 'affinity maturation', extremely strongly binding antibodies are produced. Their quantity decreases, but they protect us effectively and they also bind virus variants very well.

These immune reactions last six months or longer, not only in the case of SARS-CoV-2 infections, but also during vaccination. Much longer than the actual disease. This is also how long the antibody levels in the blood decrease. After that, however, they remain stable for many years. In the case of the first SARS virus, SARS-CoV, the antibody levels in the blood of recovered patients were stable for 17 years, from 2003/4 to 2020. This long-term stable antibody production after the end of an immune response is due to the fact that the cells that secrete these antibodies, also known as 'plasma cells', settle in the bone marrow, where they survive in certain 'niches' for many years. As an aside, the number of SARS-CoV-2-specific plasma cells in the bone marrow after surviving an infection is about the same as after being vaccinated three times with Comirnaty, and roughly corresponds to the number of plasma cells that make tetanus-specific antibodies.

#4: Saturation of the immune system.

Often heard: 'If 'sterile' immunity is so short-lived, you just have to vaccinate ('boost') more often to stimulate it again'. A misunderstanding with drastic consequences, 2G/3G regulations, shortening the 'recovered status' to a few months and a debate about compulsory vaccination. The fact is, our immune system adapts to the pathogens in our environment. With frequent contact with the same pathogen, new immune reactions no longer occur, nor does 'sterile' immunity develop. For example, protection against infection shortly after the third vaccination with Comirnaty is over 80%, after the 4th vaccination only 30%. At least when it comes to vaccination, it is not a case of 'a lot helps a lot', but rather 'enough is enough'. After all, a strong imprint of the immune system on a pathogen can also mean that we no longer react as well to new, similar pathogens (3). <<

Literature
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