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Antibody treatment for MIS-C works by depleting inflammatory immune cells

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Intravenous immune globulin (IVIG)—a common treatment for multisystem inflammatory syndrome in children (MIS-C)—likely works by depleting immune cells called neutrophils, according to a

recent study funded by the National Institutes of Health (NIH). MIS-C is a rare condition that usually affects school-age children who initially had only mild COVID-19 symptoms or no symptoms at all. The researchers also found that IVIG works in a similar manner for treating Kawasaki disease, another rare inflammatory condition that affects children and shares symptoms with MIS-C. The findings are published in the *Journal of Clinical Investigation*.

MIS-C is marked by severe inflammation of two or more parts of the body, including the heart, lungs, kidneys, brain, skin, eyes and gastrointestinal organs. Its symptoms overlap with Kawasaki disease, and treatments for MIS-C are guided in part by what is known about treating Kawasaki disease. IVIG, which is made up of antibodies purified from blood products, is a common and effective treatment for heart complications caused by Kawasaki disease. For MIS-C patients, however, IVIG alone does not always resolve symptoms, and healthcare providers may need to prescribe additional anti-inflammatory drugs.

To better understand how IVIG works and to improve treatments for children with MIS-C, researchers led by Ben A. Croker, Ph.D., and Jane C. Burns, M.D., from the University of California San Diego School of Medicine, profiled immune cells from patients with MIS-C or Kawasaki disease. The team sampled cells before treatment began as well as 2 to 6 weeks after patients received IVIG. The researchers found that neutrophils from these patients were highly activated and a major source of interleukin 1 beta (IL-1β), which is one driver of inflammation in the body. After IVIG treatment, these activated neutrophils were significantly depleted in patients with MIS-C or Kawasaki disease.

According to the study authors, their findings are the first to explain why IVIG is effective for both conditions. However, more work is needed to understand how IVIG causes cell death in these activated neutrophils and why certain patients with MIS-C require additional anti-inflammatory

treatments. Overall, the research will help healthcare providers as they determine the most effective methods to treat patients with MIS-C.

More information: Yanfang P. Zhu et al, Immune response to intravenous immunoglobulin in patients with Kawasaki disease and MIS-C, *Journal of Clinical Investigation* (2021). DOI: 10.1172/JCI147076

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