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To treat rare disease, NIH scientists repurpose FDA-approved drug

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A new study reports that a drug already approved by the Food and Drug Administration for use in patients undergoing a bone marrow transplant may also have promise for treating people who have a rare immune deficiency known as WHIM syndrome. People with the syndrome are more susceptible to potentially life-threatening bacterial and viral infections, particularly human papillomavirus infections, which cause skin and genital warts and can lead to cancer. The study was conducted by investigators at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH).

Boys and girls are equally at risk of inheriting the genetic mutation that causes WHIM syndrome, and the disorder frequently affects multiple family members. Approximately 60 patients worldwide have been diagnosed with WHIM syndrome, 10 of whom are currently receiving care at NIH.

As a result of the inherited genetic mutation, the function of a molecule, called CXC chemokine receptor 4 (CXCR4), increases. This in turn inhibits migration of neutrophils and other types of white blood cells from the bone marrow into the bloodstream. With fewer circulating immune cells, those with the disorder are less able to fight off infections.

Patients with WHIM syndrome are currently treated with intravenous immunoglobulin, a blood product containing purified human infection-fighting antibodies, and granulocyte colony-stimulating factor, a molecule that stimulates production and maturation of neutrophils. But

both therapies are difficult to administer, costly and only partially effective in treating the disease.

The drug tested in the study, known as plerixafor, blocks the activity of CXCR4 and could provide a targeted therapy for this disease. Over a seven-day period, three adult patients with WHIM syndrome were given six injections of increasing doses of plerixafor. The NIAID team observed that the numbers of nearly all immune cell deficiencies in the three patients increased to normal levels, with only minimal adverse side effects at the highest doses.

The investigators say the next step is to determine if long-term use of plerixafor, which is manufactured by Genzyme Corporation (Cambridge, Mass.), is safe and effective in adults. If it is, they will consider conducting clinical studies of plerixafor in children with WHIM syndrome.

More information: McDermott DH et al. The CXCR4 antagonist plerixafor corrects panleukopenia in patients with WHIM syndrome. *Blood*. DOI: 10.1182/blood-2011-07-368084 (2011).

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