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Pediatric hematologists introduce a novel way to treat pediatric hemophilia A patients

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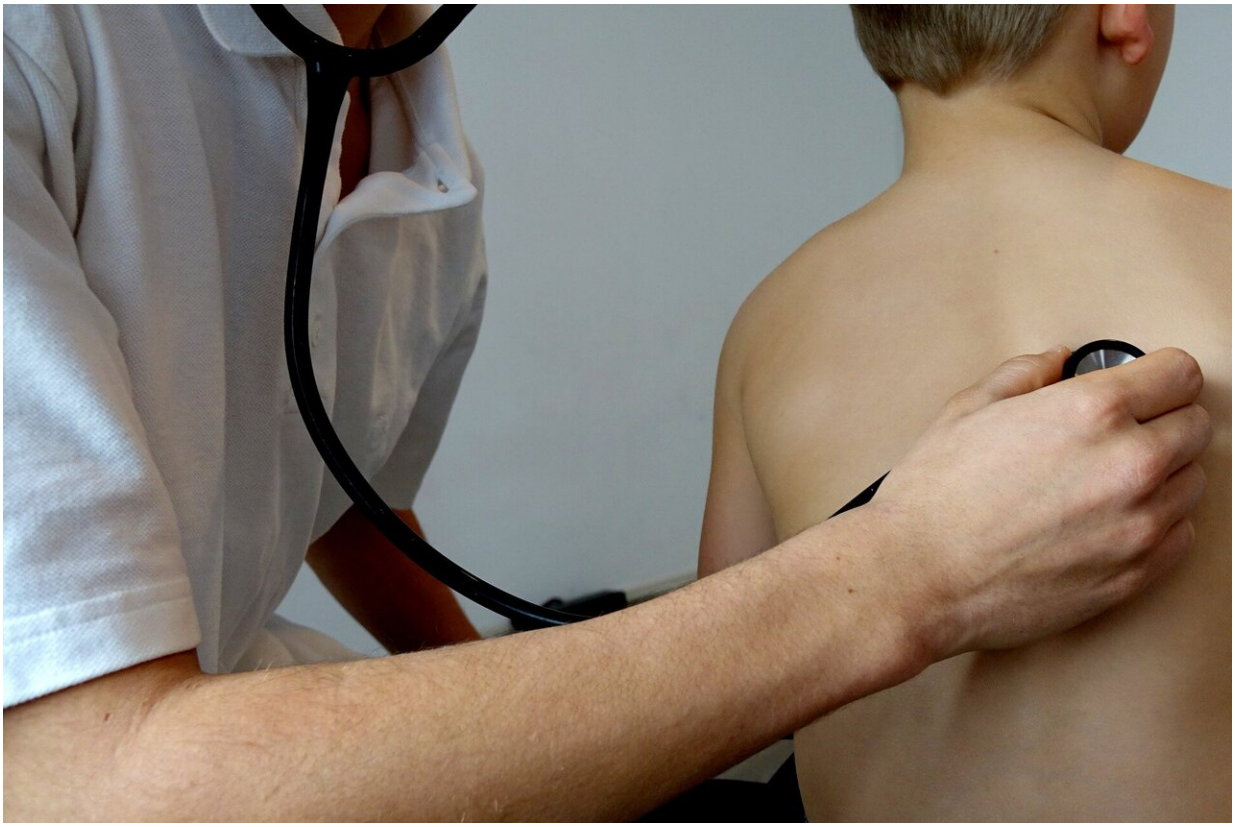

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An innovative way to treat pediatric hemophilia A patients using a combination approach has seen early success at the Aflac Cancer and Blood Disorders Center of Children's Healthcare of Atlanta, with

researchers from Emory University School of Medicine. Now known as the Atlanta Protocol, in a nod to where the approach was developed, the new method involves treating patients with high dose factor VIII concentrates along with emicizumab, a modification of the standard Immune tolerance induction (ITI).

Findings from the study were published in Haemophilia journal last month. Glaivy Batsuli, MD, assistant professor of pediatrics at Emory University School of Medicine, was first author of the publication, which was led by Children's and Emory faculty-physicians Shannon Meeks, MD and Robert Sidonio, MD.

Hemophilia, a rare bleeding and clotting disorder, affects nearly 1 in 5,000 males, and about 20,000 people in the United States have hemophilia A or B. Hemophilia A is also known as factor VIII(FVIII) deficiency. About one-third of patients with severe hemophilia A will develop antibodies directed against FVIII, called inhibitors, limiting the ability to treat hemophilia. For these patients, the immune system produces antibodies that "inhibit" clot formation by destroying the clotting factor before it has a chance to stop or prevent bleeding. Inhibitors make treating bleeds more difficult and do not allow for the standard treatment for preventing bleeds with replacement FVIII concentrates.

A relatively new drug called emicizumab, first made widely available in late 2017, mimics FVIII function by essentially tricking the body and reducing the frequency of bleeding in patients with hemophilia A with and without inhibitors. This drug can be given under the skin on a weekly, biweekly or monthly basis to prevent bleeding, rather than the intravenous infusion factor concentrates that often require a central line. The main challenge today is that, although emicizumab is very effective in reducing bleeds, it does not rid the body of the inhibitor, and ITI with FVIII concentrates remains the only effective strategy to eradicate the

inhibitor.

As a result, the pediatric bleeding disorder team at Children's led by Meeks and Sidonio offered patients the option to use emicizumab rather than traditional bypassing agents to prevent bleeding while receiving ITI. The first patients in the world to receive this new, combined treatment approach were at the Aflac Cancer and Blood Disorders Center.

Children's treats roughly 200 patients with hemophilia A, and about 30 percent of those with severe disease will develop inhibitors. Led by Batsuli, doctors collected data on seven patients included in the study—ranging in age from 21 months to 12 years old—over the course of a year. Patients were started on the novel combination of ITI with FVIII infusions three times a week and emicizumab, and followed for an average of 35 weeks. Findings demonstrated three of the seven patients completely rid their bodies of the inhibitor or reduced the inhibitor to an unmeasurable level. There were minimal bleeding events and no adverse effects such as blood clots. Six of the patients underwent surgery during this time and hospital stays decreased from the average stay of three to seven days down to one to two days.

"This study is incredibly valuable as it provides the first evidence that ITI is safe and feasible when given in combination with emicizumab," says Sidonio, associate director of the Hemostasis and Thrombosis Program at Children's Healthcare of Atlanta and assistant professor of pediatrics at Emory. "Prospective studies will be necessary to compare treatment outcomes to standard ITI regimens, but we are encouraged by the early success of the Atlanta Protocol. This new treatment will be offered to all hemophilia patients at the Aflac Cancer and Blood Disorders Center and, as a cutting-edge hemophilia treatment center, we will be sharing these results with other pediatric hospitals and institutions around the country to benefit pediatric patients nationwide."

"As the global hemophilia community began discussing how to adapt ITI in the era of emicizumab prophylaxis, our new ITI approach, the Atlanta Protocol, has been a focus," says Meeks, pediatric hematologist/oncologist at Children's Healthcare of Atlanta and associate professor of pediatrics at Emory. "We believe that this new, formalized way of tackling the problem of inhibitors can potentially improve treatment outcomes and give more hope to families living with hemophilia."

As a result of this study, two clinical trials will launch in fall 2019 to address safety and efficacy using an observational and prospective study design.

More information: Glaivy Batsuli et al. Immune tolerance induction in paediatric patients with haemophilia A and inhibitors receiving emicizumab prophylaxis, *Haemophilia* (2019). DOI: 10.1111/hae.13819

Treatment of Hemophilia A Patients With FVIII Inhibitors (MOTIVATE): clinicaltrials.gov/ct2/show/NC … nd=hemophilia&rank=1

Emicizumab PUPs and Nuwiq ITI Study: clinicaltrials.gov/ct2/show/NC … =Hemophilia+A&rank=4

Provided by Emory University