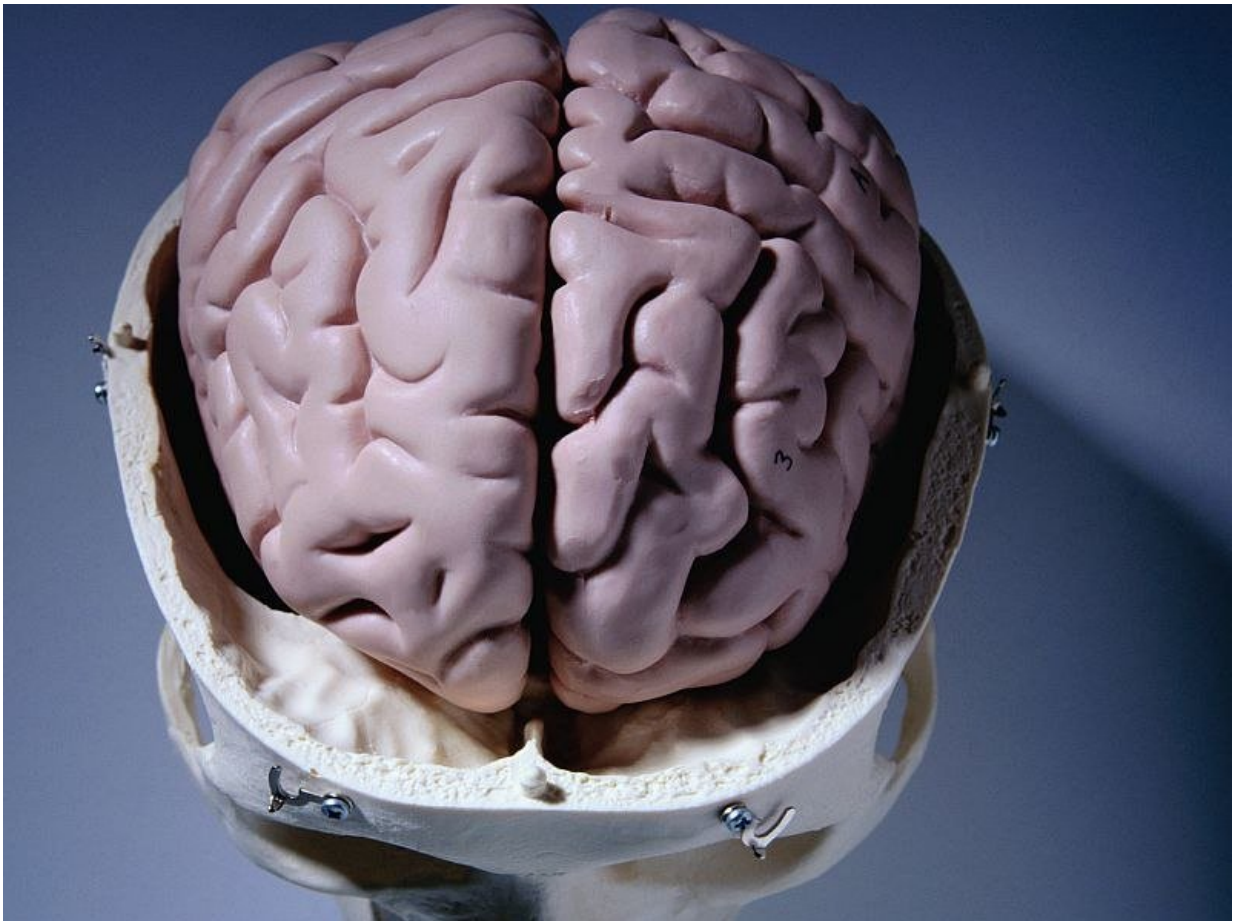


Neurotoxicity characterized after infusion of CD19 CAR-T cells

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(HealthDay)—Patients with severe neurotoxicity after infusion of

CD19-targeted chimeric antigen receptor-modified T (CAR-T) cells have evidence of endothelial activation, according to a study published online Oct. 12 in *Cancer Discovery*.

Juliane Gust, M.D., Ph.D., from the University of Washington in Seattle, and colleagues characterized neurologic adverse events in 133 adults with refractory B-cell malignancies treated with lymphodepletion chemotherapy followed by infusion of CD19 CAR-T cells.

The researchers found that there were correlations for [acute lymphoblastic leukemia](#), high CD19+ cells in bone marrow, high CAR-T cell dose, cytokine release syndrome, and pre-existing neurologic comorbidities with elevated risk of neurologic adverse events. There was evidence of endothelial activation among patients with severe neurotoxicity, including disseminated intravascular coagulation, capillary leak, and elevated blood-brain barrier (BBB) permeability. The permeable BBB did not protect the cerebrospinal fluid from high concentrations of systemic cytokines, including interferon γ , which induced brain vascular pericyte stress and secretion of endothelium-activating cytokines. The brain of a patient with fatal neurotoxicity had endothelial activation and multifocal vascular disruption. In patients who subsequently developed grade ≥ 4 neurotoxicity, biomarkers of endothelial activation were higher before treatment.

"We show [endothelial dysfunction](#) and increased BBB permeability in neurotoxicity and find that [patients](#) with evidence of endothelial activation before lymphodepletion may be at increased risk of [neurotoxicity](#)," the authors write.

Several authors disclosed financial ties to the biopharmaceutical industry, including Juno Therapeutics, which partially funded the study.

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