

Study reveals element in blood is part of human—and hibernating squirrel—stress response

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Hibernating arctic ground squirrel. Credit: Lesa Hollen/University of Alaska Fairbanks

A new study published in the journal Critical Care Explorations shows



for the first time that part of the stress response in people and animals involves increasing the levels of a naturally circulating element in blood.

The discovery demonstrates a biological mechanism that rapidly responds to severe physiologic stress and potentially serves to protect us from further damage due to life-threatening conditions.

Analyzing hundreds of <u>blood samples</u>, the researchers found that <u>iodide</u>, a form of the element iodine, increased by 17 times in <u>trauma patients</u> within two hours of experiencing severe blunt force trauma and by 26 times in sepsis patients compared with healthy donors. Using an animal model of stress—hibernation—they also discovered that iodide increases when <u>arctic ground squirrels</u> hibernate.

"The squirrels are doing the same thing as patients with life-threatening injuries: play dead but not be dead," said senior author Dr. Mark Roth, professor in the Basic Sciences Division at Fred Hutchinson Cancer Research Center.

"Our study suggests that rapid increases of iodide in the <u>blood</u> could represent an ancient response to stress that is shared across animals. If we can harness this capability it could transform emergency medicine," he said.





Hibernating arctic ground squirrel. Credit: Rhiannan Williams/University of Alaska Fairbanks

Roth's field of research explores how to put animals in a temporary <u>suspended animation</u>, like pressing pause between life and death. He was named a 2007 MacArthur fellow and received a so-called "genius grant" for his pioneering efforts.

Roth has been trying to understand how suspended animation might be used to survive near-death experiences. For example, he recalls one story of a 15-year-old who survived a trans-Atlantic flight in the wheel well of a jet dressed only in a T-shirt.



"These latest findings put us a step closer to figuring out what happened—perhaps this kid raised his blood iodide fast enough to basically hibernate before the cold and low oxygen could kill him," said Roth.

It may be odd to compare hibernating squirrels with trauma and sepsis patients, as the current study did. But what unites them is they're experiencing significant physiological stress. The study showed that, in all these groups, stress activated the same chemical responses to prevent further damage to the body.

The researchers used a blood test to see how blood iodide rose in hospitalized trauma and sepsis patients and in the hibernating ground squirrels.

The scientists also found in a mouse model that giving iodide before injury improved recovery.

They believe the protective pathway works through iodide's relationship with stress signals. Under stressful situations, iodide is released to circulate freely in the bloodstream. It acts to shield against tissue damage during stress by turning harmful hydrogen peroxide into harmless molecules of oxygen and water and reducing inflammation.

"We've known for many years that <u>stress</u>-induced inflammation makes injuries even worse," said co-author Dr. Ronald Maier, surgeon-in-chief at Harborview Medical Center, which is part of UW Medicine.

"In this study we found that iodide could provide a recyclable, effective and safe way to block damage from excessive inflammation caused by over production of oxygen radicals after injury and provides a potential therapeutic approach to enhance recovery, prevent complications and reduce mortality in severely injured patients. The use of iodide in the



clinical setting should soon be moving to clinical trials," Maier added.

Faraday Pharmaceuticals, a company founded by Dr. Roth in 2014 and led by Dr. Stephen Hill, CEO, is investigating how administering a therapeutic containing iodide may improve recovery following <u>heart</u> <u>attack</u>. The company has completed a Phase 2 study in reperfusion injury following a heart attack and is about to initiate a Phase 2 study exploring the use of iodide in ICU-acquired weakness following trauma.

In another study, Roth's team is currently looking for changes in iodide in blood samples from patients with COVID-19—a disease known to have a strong inflammatory response, called a cytokine storm. They're hoping to have results from that study later in the fall.

More information: Morrison, Michael L et al. Iodine Redistribution During Trauma, Sepsis, and Hibernation: An Evolutionarily Conserved Response to Severe Stress. *Critical Care Explorations*. September 30, 2020 - Volume 2 - Issue 10 - p e0215 <u>DOI:</u> <u>10.1097/CCE.00000000000215</u>

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