

## Inflammatory findings about cortisol

From out of nowhere, a large dog appears and lunges at you, sinking his teeth into your arm. You may not know how to react, but your body does. Almost instantaneously, you get a rush of adrenaline. At the same time, your cortisol level surges. The role of adrenaline in such a scenario is well known—it helps you to respond by either fighting back or running away. But what role does cortisol play?

A recent paper in the journal *Dose-Response* by researchers Mark Yeager, M.D., a professor of anesthesiology, Patricia Pioli, Ph.D., an assistant professor of obstetrics and gynecology, and Paul Guyre, Ph.D., a professor of physiology, begins to answer that question.

The surge in cortisol “is preparing the immune system for the subsequent challenge it might see if an infection ensues,” Guyre explains. In other words, the temporary spike in cortisol primes the body to react to a secondary threat—in this case, the possibility of an infection from the dog bite—with beneficial inflammation. The interdisciplinary team, with the aid of other scientists and clinicians, reached that conclusion after conducting several different experiments designed to decipher the relationship between cortisol levels and inflammation.

First the researchers examined the effects of lowering cortisol to below a normal (or baseline) level. Then they compared the effects of low, medium, high, and very high cortisol levels in patients undergoing cardiac surgery, a procedure that causes a lot of inflammation. And then they tested how varying levels of cortisol might prepare the body for a future infection.

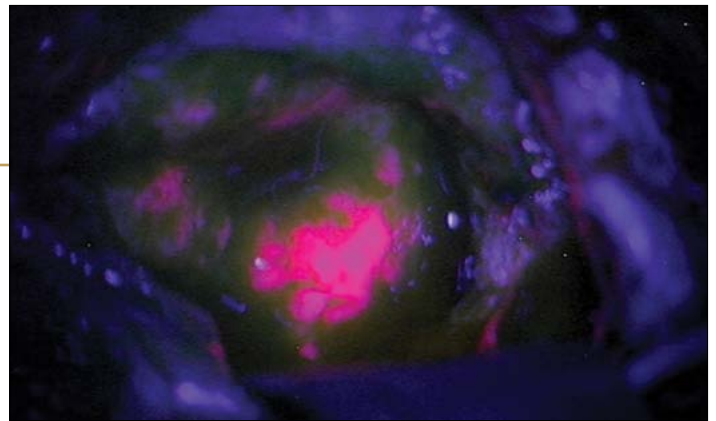
They found that the role of cortisol varies depending on the context. At normal levels, cortisol neither promotes nor suppresses inflammation. When it is at a high level during an acute, stressful event—as when facing a snarling dog—cortisol suppresses inflammation. But several hours after the jump in level, it can promote immune responses.

This dynamic portrait of cortisol is surprising given its well-known anti-inflammatory effects. Hydrocortisone cream quells the itch from poison ivy, for example, and a cortisone shot to an injured joint minimizes painful swelling.

“Because so much of human disease . . . is a complication of inflammation,” says Yeager, “all anyone wanted to think about, literally for decades,” was cortisol’s anti-inflammatory effects.

Yeager, a specialist in critical care medicine, believes that if doctors have a better understanding of how cortisol acts in the body at different times and under different circumstances, they might discover better ways to treat patients.

“Anything in which inflammation is involved could potentially be affected,” Yeager says. That includes infections from overly aggressive dogs. — Jennifer Durgin



Brain tissue during tumor surgery. The bright pink areas are cancerous tissue.

## New brain probe traces tumors

Performing surgery to remove a brain tumor requires surgeons to walk a very fine line. If they leave tumor tissue behind, the tumor is likely to regrow; if they cut out too much normal tissue, they could cause permanent brain damage.

To improve their ability to differentiate between tumor cells and healthy tissue, surgeons can have patients take an oral dose of the chemical 5-aminolevulinic acid (ALA). An enzyme metabolizes ALA, producing the fluorescent protein protoporphyrin IX (PpIX). Tumor cells have a higher metabolic rate than normal cells, so they accumulate more PpIX—and therefore glow when exposed to blue light.

But this method is often not sensitive enough to highlight brain tumors that are less metabolically active, like low-grade gliomas. To address this problem, M.D.-Ph.D. student Pablo Valdes, Ph.D., and his research mentors—David Roberts, M.D., the chief of neurosurgery at DHMC, and Keith Paulsen, Ph.D., a professor of biomedical engineering at Thayer—used a probe (which they helped develop) that combines violet-blue and white light to simultaneously analyze both the concentration of PpIX and four other tumor biomarkers: PpIX breakdown products, oxygen saturation, hemoglobin concentration, and irregularity of cell shape and size. The probe reads how light travels when it hits the tissue, sends this data to a computer, runs it through an algorithm, and produces a straightforward answer as to whether the tissue is cancerous.

In a pilot study, Roberts operated on 10 patients with gliomas. He used a microscope throughout the surgery to see the fluorescence and used the hand-held probe to evaluate sections of the tissue where the fluorescence was not definitive. After the surgeries were complete, a pathologist evaluated how accurately the probe had identified tumor tissue.

The results, published in the *Journal of Biomedical Optics*, are striking. Diagnoses based on only fluorescence had an accuracy of 64%. But when Roberts used the probe as well, the accuracy increased to 94%, meaning that Roberts was much more successful in differentiating between tumor tissue and normal tissue. Although the study was small, it introduces a promising method to help surgeons remove only what they want and nothing more. — Alannah Phelan

**The temporary spike in cortisol primes the body to react to a secondary threat.**