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(Last updated 7/26/99)

Previous Ohio State research stories about the link between stress and immunity:

[Stress May Increase Susceptibility To Infectious Disease](#), 7/23/99

[New Hypothesis Proposed for Cause of Chronic Fatigue Syndrome](#), 10/28/98

[Stress Slows Healing Of Dental Wounds By 40 Percent](#), 6/17/98

[Stress of Breast Cancer Surgery, Diagnosis Weakens Immune System](#), 1/20/98

[Marital Arguments Lead To Weakened Immune Systems In Older Couples](#), 8/14/97

[Psychological Stress Can Slow The Rate of Wound Healing](#), 4/22/97

[Effects of Arguments Linger Long After Fights End, Study Shows](#)

RESEARCH NEWS



7/23/99

RESEARCHERS LEARN HOW STRESS SLOWS WOUND HEALING

COLUMBUS, Ohio -- Scientists investigating why wounds heal more slowly on patients who are stressed have found that psychological stress can increase the levels of some hormones in the blood.

These hormones can slow the delivery of certain compounds -- cytokines -- to the site of the injury to start the healing process.

But if the process is slowed at the beginning, the wound will take much longer to heal, posing potentially serious consequences to patients recovering from surgery.

This finding, reported in a recent issue of the *Archives of General Psychiatry*, is the latest clue to how psychological stress causes physiologic changes within the body, many of which can weaken a person's health.

"There is a lot in the medical literature suggesting, if possible, that a patient should not be under stress before surgery," explained Jan Kiecolt-Glaser, professor of psychiatry and psychology at Ohio State University. "Stress, depression and anxiety prior to surgery have all been associated with poor surgical recovery."

The problem, she said, is that while physicians have known about this problem, they didn't understand exactly how stress could alter the healing process. This study was an attempt to identify clues to the cause.

Ronald Glaser, professor of medical microbiology and immunology and lead author of the paper, and Kiecolt-Glaser assembled a group of 36 women for the study at the university's Institute for Behavioral Medicine Research. Each of the women was asked to complete three questionnaires intended to gauge their levels of stress. They were then admitted to Ohio State's General Clinical Research Center (GCRC).

4/22/97

[High Stress Weakens Immune Function In Breast Cancer Patients](#), 3/11/97

Researchers then applied a mild suction to the forearms of each woman which caused the upper layers of skin to separate, creating eight minor blisters, each the size of a pea. This procedure was relatively painless, causing little stress.

The researchers removed the skin topping each blister, covered the wound with plastic and then filled the small blister "well" with a sterile solution. The wounds were then sealed.

After five hours, the fluid at four of the blister sites was removed for testing. Fluid was taken from the remaining four blisters after 24 hours. The samples were then analyzed. Researchers also took samples of saliva from each of the women at the start of the experiments, at five hours and at 24 hours to gauge the concentration of the hormone cortisol.

The researchers were looking for concentrations of two cytokines -- IL-1 and IL-8 -- along with specific cells called neutrophils, essential for repairing injured tissue. As expected, an analysis of both the five-hour and 24-hour samples showed the number of neutrophils at the wounds had increased dramatically so stress appeared to have no impact on cells reaching the wound site.

But the analysis showed that women who had reported more stress before the experiments produced significantly lower levels of both cytokines, Kiecolt-Glaser said. Those same women showed higher levels of the hormone cortisol in their saliva. Cortisol plays an important role in curtailing the healing process -- higher cortisol levels can lead to a slowdown in healing.

"When we looked at the levels of cortisol in the saliva and compared them to the levels of both cytokines, we saw the kind of correlation we would expect if the immune response was being affected," explained William Malarkey, professor of internal medicine and director of GCRC.

Malarkey said that normally, when levels of cortisol increase, it suppresses the immune response. It either reduces the number of neutrophils that rush to the wound site or it controls the concentration of the cytokines necessary for healing.

"It's important to note that the women in this experiment were really average in terms of the stress they were experiencing," Kiecolt-Glaser said. "So this doesn't require desperate, terrible stress levels to see effects on the immune system."

Kiecolt-Glaser said that patients anticipating surgery probably have stress levels much higher and therefore, are at greater risk when it comes to proper wound healing. And people suffering from clinical depression are probably at much higher risks of poor healing.

The next step, the researchers say, is to do comparative studies testing if certain intervention activities intended to reduce stress will also speed up the healing process.

Philip Marucha, associate professor of periodontology; Robert C. MacCallum, professor of psychology; and Bryon Laskowski, research associate in medical microbiology and immunology, were part of the research team on this project, which was sponsored by the National Institutes of Health.

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