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# Kiecolt-Glaser Offers New Paradigm on How Stress Kills

**By Belle Waring**

**Photos by Ernie Branson**

**On the front page...**

The idea that the mind affects health and illness is thousands of years old, but only in recent decades have scientists tracked down the data.

Now Ohio State University's Dr. Janice Kiecolt-Glaser is adding to the growing evidence on the health consequences of stress. In her talk "How Stress Kills: New Perspectives on Stress and Inflammation," she offered recent findings to a packed house in Lipsett Amphitheater.

"She has done seminal work in a field with a long name," said NIDCR's Dr. Nadya Lumelsky in her introduction. That field is psychoneuroimmunology, the interdisciplinary study of brain, mind and immune system. "There was lots of anecdotal evidence, but Dr. Kiecolt-Glaser has shown a causal relationship between stress and other diseases."

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Dr. Janice Kiecolt-Glaser

A clinical psychologist, Kiecolt-Glaser collaborates with her husband, virologist Dr. Ronald Glaser, at OSU's Mind/Body Center, and has received support for 3 clinical trials from NCI, NCCAM and NIA. She was invited to speak by NIDCR as part of its translational seminar series.

How do scientists prove the effects of stress on health? One path is to follow the cytokines, among the most crucial proteins in the body. Cytokines, including the interleukins, carry messages vital to immune response. Part of that response is inflammation. As one of the body's normal defenses against infection, injury, irritation or surgery, inflammation is not the same as infection. And acute inflammation is not the same as chronic.

"We need good inflammation," said Kiecolt-Glaser, "because cytokines attract immune cells. With acute inflammation, good things happen. With chronic inflammation, you have troubles, because of its association with tumor cell survival" and other harms.

It's an intricate process. Imagine tumbling down a ladder in a cascade of negative effects:

- Chronic stress can cause immune dysregulation.
- This dysregulation causes increased risk of disease.
- And that risk in turn increases the proinflammatory cytokines, including interleukin-6 (IL-6).

Kiecolt-Glaser's studies show that "you can skip all the steps and go directly from stress to cytokines."

Some highlights on how chronic stress affects health:

- Chronic stress substantially accelerates age-related changes in IL-6, a cytokine linked to some cancers, cardiovascular disease, type II diabetes, osteoporosis, arthritis, frailty and function decline. "It's a new

paradigm," Kiecolt-Glaser said. "Cholesterol and the immune system work together to cause heart disease and stroke."

- At 71 or older, age interacts with stress, and "the older you are, the more stress really matters." It impairs vaccine responses in older adults.
- Turning to the young: When dental students on vacation were compared to those taking "a particularly dreaded exam—immunology," no student healed as rapidly during exams. Oral wound-healing took them 40 percent longer.
- Personal relationships influence immune/endocrine function and health. Hostile couples' wounds healed more slowly after conflict.
- Women show larger response to interpersonal stress.
- In caregivers (for example, spouses caring for their aging/ailing mates) the average rate of increase for IL-6 was about 4 times larger than that of non-caregivers.

Chronic stress increases proinflammatory cytokines, says OSU's Kiecolt-Glaser.

"What happens when caregiving ends?" an audience member queried.

"Normal bereavement decreases after 2 years," said Kiecolt-Glaser. "It doesn't create a change in mood, long term."

But for those exhausted by extended caregiving, "they lose part of their social networks, becoming increasingly depressed. You lose part of your life."

A vicious cycle takes hold. "Patients with major depression will have even more depressive symptoms. The stressed get more stressed, serving as substrate for more inflammation. They are primed to respond more strongly to subsequent challenges."

And although we know we're supposed to take care of ourselves, "what we tend to do is to turn to high-fat diet, less exercise, poor sleep and smoking," she said. "Stress promotes poor health behaviors...and sleep is one of the first things to go. If you didn't sleep well last night, your IL-6 is higher today."

Meanwhile, "Adipose belly fat secretes as much as three times the level of IL-6. Those fat cells act like little IL-6 factories."

Moderate physical activity can help attenuate inflammation, she said. "Of course, when you're stressed, that's the last thing you want to do."

Kiecolt-Glaser is also investigating the ability of omega-3 fatty acid supplementation to alter mood and inflammation.

There is, of course, good fat and bad fat. The history of dietary changes, along with epidemiological evidence, shows that "countries that eat more fish are better off," she said. Also healthful are fish oil, walnuts, wheat germ and flax seed.

There is also the correct ratio of different types of fatty acids—in this case, omega-3 and omega- 6. That ratio is implicated in depression, cardiovascular disease and inflammation.

"This is nutritional neuroscience and psychoimmunology: interdisciplinary science at the crossroads," she said. Depressive symptoms interact with diet to enhance inflammation. During Q&A, an audience member asked: When it comes to the stress of caregiving, does the individual have any control?

A big theme is the lack of control, she said. Changes in a spouse's health status can be unpredictable and are some of the worst stressors, since treatments can be "hard to implement in real life."

Her ongoing work includes how mind-body interventions such as yoga may modulate endocrine and immune responses.

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