EVERYONE KNOWS WHAT IT’S LIKE TO BE lonely. It often happens during life’s transitions: when a student leaves home for college, when an unmarried businessman takes a job in a new city, or when an elderly woman outlives her husband and friends. Bouts of loneliness are a melancholy fact of human existence.

But when loneliness becomes a chronic condition, the impact can be far more serious, says John Cacioppo, a social psychologist at the University of Chicago in Illinois. Cacioppo studies the biological effects of loneliness, and in a steady stream of recent papers, he and collaborators have identified several potentially unhealthy changes in the cardiovascular, immune, and nervous systems of chronically lonely people. Their findings could help explain why epidemiological studies have often found that socially isolated people have shorter life spans and increased risk of a host of health problems, including infections, heart disease, and depression.

Their work also adds a new wrinkle, suggesting that it’s the subjective experience of loneliness that’s harmful, not the actual number of social contacts a person has. “Loneliness isn’t at all what people thought it was,” Cacioppo says.

Colleagues credit him with building an impressive network of collaborations with researchers in other disciplines to pioneer a new science of loneliness. “He’s placed it on the scientific map,” says one collaborator, Dorret Boomsma, a behavioral geneticist at Vrije Universiteit Amsterdam in the Netherlands. “He’s doing very creative work,” says Martha Farah, a cognitive neuroscientist at the University of Pennsylvania. “He’s created a new way of thinking about the biology of interpersonal relationships.”

A new beginning
Cacioppo hasn’t always studied loneliness. In the 1980s and ’90s, he made a name for himself with meticulous laboratory studies on various aspects of emotion and cognition, and he’s a founder of the field of social neuroscience, which seeks to understand the brain’s role in social behavior. (Last month, colleagues elected him president of the newly formed Society for Social Neuroscience.)

Cacioppo says a 1988 Science paper suggesting that social isolation increases mortality (29 July 1988, p. 540) prompted him to change the focus of his research. Since then, scores of studies have found that people who lack social support are more prone to a variety of ailments. An analysis of 148 of these studies, published in the July 2010 issue of PLoS Medicine, suggests that social isolation increases the risk of death about as much as smoking cigarettes and more than either physical inactivity or obesity.

Compelling as these epidemiological studies are, Cacioppo says, they leave unanswered many questions about the mechanisms involved and about what aspects of social isolation are responsible. In the early 1990s, he set out to tackle these questions. He began by handing out questionnaires to thousands of students at Ohio State University in Columbus, where he was based at the time, and following up with physiological and psychological testing in the lab. For the past 10 years, he has been testing hundreds of Chicago-area residents, working closely with psychologist Louise Hawkley and other University of Chicago colleagues.

This work has convinced Cacioppo that
loneliness is a health risk on its own, apart from conditions such as depression or stress that are common fellow travelers. More specifically, it seems to be the subjective experience of loneliness that’s important for people’s well-being rather than any objective measure of social connectivity (the number of close contacts someone has, for example). It’s an important distinction that most previous studies had ignored, says Daniel Russell, a psychologist at Iowa State University in Ames. “Some people are socially isolated and they’re not lonely,” Russell says. “By contrast, some people are lonely even if they have a lot of social contacts.”

As a graduate student in the 1970s at the University of California, Los Angeles (UCLA), Russell helped develop the scale Cacioppo now uses in most of his research. The UCLA Loneliness Scale is based on a questionnaire that tries to size up how people perceive their social situation, with questions about how often they feel a lack of companionship, feel they have no one to talk to, or feel out of tune with those around them.

**Sympathetic feelings**

When people score high on the UCLA Loneliness Scale, Cacioppo and colleagues have found, they also tend to exhibit several physiological changes that effectively put the body in a state of alert. In one early study, they found that lonely people exhibit higher vascular resistance, a tightening of the arteries that raises blood pressure. That forces the heart to work harder and can contribute to wear and tear on vessels.

“Those were landmark investigations” that got other researchers interested in potential biological effects of loneliness, says Chris Segrin, a behavioral scientist at the University of Arizona in Tucson.

Lonely people also have elevated molecular markers of stress. Cacioppo’s group has found that cortisol and epinephrine are elevated in saliva and urine, respectively. That might help explain why lonely people report feeling more stressed in situations most people experience as only moderately stressful, such as public speaking, Cacioppo says.

Together, these findings point to activation of the sympathetic nervous system, which coordinates the body’s fight-or-flight responses. It’s as if loneliness prepares the body for some looming threat. Cacioppo thinks that makes evolutionary sense. He argues that being alone, for our distant ancestors, meant abandoning the protection of the group and jeopardizing one’s genetic contribution to the next generation. He posits that the physiological changes and anxiety that accompany loneliness are a warning that an individual’s social ties have gotten too weak. “It’s an aversive signal that motivates us to change our behavior in a way that’s good for our genetic survival.” In his view, loneliness is a double-edged sword—adaptive in the short term but dangerous when it becomes chronic.

Cacioppo and colleagues have also found evidence that loneliness has a direct impact on the immune system. In a 2007 study in *Genome Biology*, Cacioppo teamed up with UCLA genomics researcher Steve Cole and other colleagues to investigate gene activity across the genome in the white blood cells of 14 participants in a longitudinal study of loneliness among Chicago-area residents. The volunteers selected scored in either the top or the bottom 15% of the study cohort on the UCLA Loneliness Scale.

Two differences between the groups stood out: Lonely people exhibited increased activity for several genes encoding signaling molecules that promote inflammation and decreased activity for genes that normally put the brakes on inflammation. They also showed diminished activity in genes that help mount a defense against viral invaders.

Cole says that jibes with epidemiologic findings that socially isolated people are more susceptible to viruses, from the common cold to HIV, and to cardiovascular disease, which has been linked to excess inflammation. Cole says the team will soon publish a replication of the findings in a group of about 120 participants in the Chicago study. He notes that just feeling a little left out isn’t likely to throw the immune system out of whack. “It really takes a person who has taken and consolidated a lonely view of the world to show these changes in gene expression,” he says.

Loneliness not only increases wear and tear by keeping the body in alert mode but also may prevent people from recharging their batteries with rest and relaxation. In the March 2010 issue of *Health Psychology*, Cacioppo and colleagues reported that although lonely people sleep a normal number of hours, they report more fatigue.
the next day, suggesting that their quality of sleep isn’t as good. Segrin says his group has recently replicated this finding and extended it to show that lonely people derive less satisfaction from leisure activities. Their findings are in press at *Health Communications*.

**The lonely brain**

Studies by Cacioppo and others before him have found that lonely people tend to rate their own social interactions more negatively and form worse impressions of people they meet. Researchers are beginning to show how these biases may be encoded in the brain. In a 2008 study in *The Journal of Cognitive Neuroscience*, Cacioppo and colleagues used functional magnetic resonance imaging to measure metabolic activity in the brains of 23 undergraduate women at the University of Chicago. Those who were lonelier, as rated by the UCLA Loneliness Scale, exhibited less activation in the ventral striatum, a component of the brain’s reward circuitry, when they viewed pictures of smiling faces.

In another study, Cacioppo and colleagues asked lonely and nonlonely people to perform the Stroop test, a workhorse task in experimental psychology in which people see words presented in colored text one by one on a computer screen, then indicate what color they feel to be alone,” Cacioppo says. The news isn’t all bad, however. Even for hard cases, Cacioppo believes loneliness can be overcome. He and colleagues recently conducted a meta-analysis of 20 studies on interventions for loneliness. Simply providing social support doesn’t seem to work, especially if people know they’re being looked after. “If you know people are stopping by to check on you, it makes you feel like more of a loser,” Cacioppo says. The most effective interventions were those that borrowed methods from cognitive behavioral therapy to shift people’s attention and interpretation of social situations in a more positive direction, the team reported online 17 August 2010 in *Personality and Social Psychology Review*.

As for preventing loneliness, Cacioppo says it helps to know where your own thermostat is set and strive to stay in your comfort zone. In *Loneliness*, he writes: “The degree of social connection that can improve our health and our happiness … is both as simple and as difficult as being open and available to others.”