

Stressed Out

Medical journals don't frequently publish papers by social scientists. But two of the world's most prestigious medical journals made an exception for Sheldon Cohen. The Carnegie Mellon psychology professor's research on stress could help prompt changes in the way physicians practice medicine.

by Jennifer Bails





The roar of jet engines is an ear-popping reality at this elementary school beneath a common flight path to Los Angeles International Airport. More than 300 airplanes pass overhead daily—including one jumbo jet every 2.5 minutes during school hours. Certainly, the noise must be irritating and unpleasant to the students.

A young psychologist wonders whether something more insidious is happening. During his undergraduate studies as a psychology major, Sheldon Cohen stumbled upon a conjecture that noise in urban environments might impair reading ability in children. He has found an ideal real-world laboratory to explore the theory.

First, Cohen takes decibel readings throughout the school. Then, he measures reading performance in the children and assesses their ability to distinguish between similar words. Results show that the students appear to have adapted by tuning out the noise but, in turn, haven't learned to discriminate between speech sounds that are requisite for reading. Not surprisingly, he discovers that noise exposure also is associated with problem-solving deficits and feelings of helplessness.

Yet another pattern emerges from the data that is unusual—and even more intriguing to Cohen: The children attending school under the air corridor to LAX also have higher than normal blood pressure levels. He mulls over the problem of mind-body connection—that is, how a psychological stressor such as chronic noise could “get under the skin” to influence a biological factor like blood pressure.

If stress can elevate your blood pressure, he wonders, what other health effects might it have? Could feeling stressed make you more susceptible to colds? Or what about more serious illnesses—heart attacks, depression? Ask your neighbor or best friend any of these questions, and intuitively, they would probably answer “yes.”

“People on the street are easy to ac-

cept these things,” says Cohen, now the Robert E. Doherty Professor of Psychology at Carnegie Mellon. “But they turn out to be a lot harder to prove.”

Until very recently, the biomedical community has remained skeptical that stress is a risk factor for disease. “It is such a popular topic with the lay public that it caused the scientific community to be anxious—or frankly, stressed—about looking at this field,” says stress expert Esther Sternberg, chief of the Section on Neuroendocrine Immunology and Behavior at the National Institute of Mental Health. “The area got a bad rap as being soft science.”

That reputation is changing, in no small part owing to Cohen’s work to bring the rigors of the scientific method to the study of stress. Those efforts began in earnest with his classic noise studies almost 30 years ago. Since then, Cohen has published more than 150 journal articles and book chapters, received millions of dollars in federal research grants, and been elected to the National Academy of Sciences’ Institute of Medicine.

“Sheldon Cohen is a pioneer—if not *the* pioneer—in looking at the relationship between stress and disease,” Sternberg says. “He really was one of the first people to bring some solid scientific methodology into the field. It created a firestorm of great excitement.”

Only after decades of research is Cohen convincing the medical community that stress isn’t merely a benign complaint. It really matters in ways that are more powerful and pervasive than even he ever imagined.

Watertight clinical evidence linking stress to disease has been elusive—partly because stress is so personal and unpredictable, making it difficult to quantify and measure its impact. Rush hour. Deadlines. Caring for a sick loved one. Bills. Job changes. Colicky babies. Divorce. Chores. Loud neighbors. Demands, demands, demands. “Stress is an unavoidable consequence of life,” says Paul Rosch, president of the American Institute of Stress and psychiatry professor at New York Medical College. “Without stress there would be no life.”

But in studying the relationship between stress and disease, it is difficult to separate cause from effect, says Anna Marsland, Cohen’s longtime collaborator and assistant professor of psychology at the University of Pittsburgh. For example, are stressed people more likely to get a postnasal drip because they seek solace from friends and family, thereby widening their exposure to germs? Or perhaps they withdraw from others, sleep and exercise less, and smoke and drink more—behaviors that don’t exactly promote good health.

In 1982, when Cohen joined the psychology department at Carnegie Mellon, evidence was accumulating to suggest that stress could alter immune response. It was still unclear, though, whether its effects on immunity were enough to compromise the body’s ability to fight infection.

Cohen set out to answer those questions. To conduct the research, he needed to become well versed in virology, immunology, and endocrinology. A 15-year career development award from the National Institute of Mental Health allowed him to pursue his goal. In the course of his studies, he met David Tyrell, a virologist who ran the Common Cold Unit in England.

That unit was established by Britain’s Medical Research Council in 1946 to find the cause and treatments for the common cold. Although he never found a cure, Tyrell discovered much of what we know today about cold viruses. Central to his research were trials in which healthy volunteers were inoculated with a cold virus and then quarantined so they could be monitored closely for infection and illness.

Cohen saw a perfect opportunity to piggyback on Tyrell’s experiments to determine whether stress predicts who develops colds. In his landmark study at the Common Cold Unit, he had almost 400 subjects complete exhaustive questionnaires that assessed degrees of stress. Next, they were given nasal drops of a cold virus and observed for a week in a controlled environment. Cohen found that the higher the score on his stress in-



Cohen squeezes the stress out of his day.

dex, the greater the probability of catching a cold following viral exposure.

It was the first time research provided scientific proof that stress, independent of the unhealthy behavior it causes, is associated with susceptibility to illness. The results, says Marsland, were groundbreaking. “The real beauty of Sheldon’s work is that it is very experimental and systematically controlled so that we can draw clear conclusions about the impact of stress on vulnerability to infection.”

Cohen’s findings appeared in August 1991 in the *New England Journal of Medicine (NEJM)*, the oldest continuously published medical journal in the world. The peer-reviewed journal publishes new research findings on topics of importance to biomedical science and

clinical practice. Historically, it declines to publish results of behavioral studies.

“I had no idea how difficult it is to publish a paper in that journal or how nearly impossible it is to publish anything about psychosocial predictors of health,” Cohen says. “I think if I knew then what I do now, I might never have sent it in.”

Cohen’s *NEJM* article helped to initiate more than 20 years of common cold studies at his laboratory at Carnegie Mellon. Using the same experimental paradigm as he had in Britain, he has determined that just any old stress will not do when it comes to putting people at risk for colds—it has to last at least a month and stem from interpersonal troubles like marital strife or enduring job-related problems.

“That was disappointing,” he says. “We thought once we knew what kind of stressors matter, we could isolate them and do some kind of intervention, but when the stressor is a bad marriage or a lousy job, what are we going to do?” He decided to delve deeper into the body in search of explanations for how chronic stress acts to recalibrate our physical machinery.

It is known that stress elevates levels of cortisol. The stress hormone is part of the “fight-or-flight” response. Blood pressure and heart rate increase to prepare for action. The immune system is suppressed as the body concentrates on coping with the present danger rather than maintaining long-term health. The response can be lifesaving in a sudden attack, but it is damaging to the body when activated chronically.

Unexpectedly, Cohen found that the impact of stress on health risk was independent of the hormone response. He believes that hormones still matter, albeit in a less direct way.

What he recently discovered is that prolonged stress interferes with the body’s ability to turn off production of pro-inflammatory cytokines. The messenger proteins are produced by the immune system in response to infection. The cytokine outpouring to a viral infection—not the virus itself—elicits

the symptoms of a cold. It is a matter of delicate balance. Too little cytokine, and you can’t fight off infection. Too much cytokine, and you still feel sick.

Here is where cortisol comes into play again. One of the functions of the stress hormone is to turn off cytokine production. But if there is too much cortisol in circulation, the hormone can’t do its job. That means people who are chronically stressed, producing oodles of cortisol, also have excess cytokine, in turn triggering and prolonging a cold.

Last year, the Institute of Medicine, impressed with Cohen’s body of research, commissioned him to examine the evidence that stress also influences major diseases. His resulting article, co-written by Carnegie Mellon postdoctoral fellow Denise Janicki-Deverts, appeared in an October issue of the *Journal of the American Medical Association (JAMA)*, the world’s most widely circulated peer-reviewed medical journal.

“For a lot of years, I’ve been writing about stress and disease, and we actually know a lot in some areas, but that knowledge hasn’t gotten across to the medical community in some coordinated way until now,” Cohen says.

The article details a critical mass of studies indicating that stress plays a role in causing or worsening depression and heart disease and in speeding the progression of HIV to AIDS.

Such accumulation of clinical evidence linking stress with diseases is growing hard for the medical community to ignore. The very appearance of articles by Cohen, a psychologist, published in mainstream medical journals such as *JAMA* and *NEJM* suggests that physicians are starting to recognize that biology alone cannot explain all aspects of illness.

“The skepticism is decreasing, and there really is a belief and interest in the role of psychological factors like stress,” Marsland says. Cohen and his colleagues want more time, thought, and dollars invested to explore which interventions might reduce stress and whether those strategies then translate into less disease. They also are calling upon clinicians to

include the diagnosis and treatment of stress in their routine patient care.

The National Institute of Mental Health’s Sternberg urges people with demanding, stressed-filled lives to “do something about it” right now. She suggests people pace themselves at work and take up relaxing exercises such as swimming, walking, or Tai Chi. Most importantly, she says, people should seek support from those who care about them.

“Don’t try to do this on your own,” she recommends.

Cohen particularly agrees with Sternberg’s last bit of advice because he has uncovered substantial evidence that social support can act as a buffer against the dangers of stress. The belief that others are there to provide the extra help you need can bolster your perceived ability to cope with demands and make your problems seem less daunting, explains Cohen.

He applies the findings to his own life. As a high-profile research scientist and active teaching professor, Cohen certainly experiences his fair share of stress. Right now, he is embarking on new projects to explore links between stress and aging and studying whether positive emotions impact well-being. In addition, through participation in a MacArthur Foundation research network, he is trying to understand how childhood socioeconomic status affects health.

Some relief from those demands comes from gardening and playing golf, when time—and his aching back—allow it. Cohen, married to professional dancer and choreographer Mary Miller, tries to surround himself with loved ones, friends, and co-workers to further absorb the blows of stress.

“I don’t have any magic pill,” he says. “I can tell you what my doctor says—‘Reduce your stress.’ I always find it amusing when he tells me this.” ■

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