NEWS

Stress

BY **JERRY ADLER** 6/13/99 AT 8:00 PM

1) IMMEDIATE
IN RESPONSE TO A PERCEIVED THREAT, THE BODY CHANNELS RESOURCES FOR STRENGTH AND SPEED.
WITH CLAUDIA KALB AND ADAM ROGERS

Brain Stress protectively dulls the body's sense of pain. Thinking and memory improve.

Eyes The pupils dilate for better vision

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Lungs The lungs take in more oxygen

Liver Sugar stored as glycogen is converted to glucose

Heart The bloodstream brings extra oxygen and glucose--fuel--for power. Heart rate and blood pressure rise.

Adrenal glands The medulla secretes fight-or-flight hormone epinephrine (adrenaline)

Spleen Extra red blood cells flow out, allowing the blood to carry more oxygen to muscles

Intestines Digestion halts, allowing the body to dedicate energy to the muscles

Hair Body hairs become erect-puffed-up hair makes animals look bigger and more dangerous

2) Delayed
A few minutes after the fight-or-flight response, the body makes other changes to stabilize and replenish itself.

Brain The hippocampus, a center of memory and learning, gets activated to process the stress

Immune system Infection-fighting is diminished, perhaps increasing available energy

Liver Fat-stored energy-is converted into usable fuel

Adrenal glands The cortex secretes cortisol, which regulates metabolism and immunity. Over time, though, it can be toxic.

3)Chronic
If activated too often, the stress response may harm the immune system, brain and heart.

Brain Cortisol becomes toxic to brain cells, potentially damaging cognitive ability. Fatigue, anger and depression increase.

Immune system Repeated suppression of disease-fighting cells ultimately weakens resistance to infection

Intestines Decreases in blood flow leave mucous lining vulnerable to ulcers

Circulatory system Elevated blood pressure and heart rate damage elasticity of blood vessels

Stress isn't just a catchall complaint; it's being linked

to heart disease, immune deficiency and memory loss. We're learning that men and women process stress differently and that childhood stress can lead to adult health problems. The worst part is, we inflict it on ourselves.Children who were neglected by their parents or raised in orphanages tend to have higher levels of stress hormones and may be 'hot reactors' later in life. As adults, they may feel empty or bored when not on edge.Though a man's blood pressure rises more sharply in response to stress, women react to a wider range of stressors and say they feel stress more often, perhaps because they take a holistic view of everyday life.

By Jerry Adler

It was vital to survival once--an innate response to danger, inherited directly from the primeval veld down to our own lifetimes, where it causes nothing but trouble. Some people make a virtue of stress, under the mantra "that which does not kill me makes me stronger." But science shows this to be a lie. A whole new body of research shows the damage stress wreaks on the body: not just heart disease and ulcers, but loss of memory, diminished immune function and even a particular type of obesity. That which doesn't kill you, it turns out, really does kill you in the end, but first it makes you fat.

Zen masters, of course, have known this for a long time, and techniques such as yoga are still useful prescriptions for stress (following story). But orthodox Western medicine long resisted the notion that a purely mental condition could have measurable effects in the empirical realm of arteries and organs. "When I started studying stress 30 years ago, I was told I was jeopardizing my medical career," says Dr. Herbert Benson, who founded the Mind/Body Medical Institute at Harvard. It was only in the past few years that researchers came up with a quantifiable measure of stress, based on the concentration of certain hormones in saliva, and began tracing the complex neurological and chemical events that lead from a traffic jam on the Santa Monica Freeway to cardiac

intensive care at Cedars-Sinai. Research has revealed that men's and women's bodies process stress differently, and provided disturbing evidence about how stress affects child development from the earliest weeks of life. And it has spawned a whole new discipline, psychoneuroimmunology--which, according to Bruce Rabin of the University of Pittsburgh, has reached the point where research on smoking and cancer was back in the 1960s. "You knew there was a link because of the epidemiology, but you didn't know the mechanism. Now there's enough epidemiology to establish the association [between stress and illness]. We're still working out the mechanisms."

The very concept of stress was formulated only in the 1930s, by the pioneering endocrinologist Hans Selye. It was Selye's insight that organisms show a common biological response to a wide range of unpleasant sensory or psychological experiences. These are called "stressors." Stressors are, in shorthand, whatever you're trying to avoid: an electric shock, if you're a lab rat; the sight of a predator, if you're a prey animal; a 500-point drop in the Dow, if you're a Yuppie. Those are acute stress events; everyone recognizes the adrenaline rush (pounding heart, dry mouth, butterflies in the stomach) that marks their onset. Human beings are equipped to deal with it, if it doesn't happen too often. But when it happens again and again, the effects multiply and cascade, invisibly, compounding over a lifetime.

The classic study linking stress to immune dysfunction was done just in 1991, when Carnegie Mellon psychologist Sheldon Cohen and his colleagues showed that people who ranked high on a psychological test of perceived stress were more likely to develop colds when intentionally infected with a respiratory virus. He repeated the study last year and this time refined his results: although a single, large, stressful event in the preceding year did not affect the subjects' chances of getting sick, chronic stress--ongoing conflicts with co-workers or family members, for example--increased the odds by as much as three to five times. Looking at another measure of immune function, response to a standard influenza vaccine, immunologist Ronald Glaser of Ohio

State found diminished antibody production (compared with a control group matched for age) among people caring for a spouse with dementia. "The human body," says Dr. Pamela Peeke of the University of Maryland, "was never meant to deal with prolonged chronic stress. We weren't meant to drag around bad memories, anxieties and frustrations."

Other studies (chart) have found an association between long-term stress and heart problems. That's also true of macaque monkeys, favored subjects of stress researchers because they share with humans a hierarchical social structure and a susceptibility to coronary-artery disease. Wake Forest University anthropologist Jay Kaplan studied both high- and low-status male macaques in captivity, and found, as expected, that the subordinate ones showed more atherosclerosis. But when he artificially shook up the social hierarchy, by introducing new animals into the troop, it was the high-ranking males, forced to fight again and again to establish their dominance, who showed the most signs of coronary disease.

Yet the stress reaction obviously serves an evolutionary purpose. It is, essentially, a response to danger, in two distinct phases. The first of these, involving the "sympathetic-adreno-medullary axis" (SAM), is the familiar flight-or-fight response. Your brain perceives a threat--a lion crouched in the brush is the classic illustration--and sends a message down the spinal cord to the medulla, or core, of the adrenal glands (chart), signaling it to pump out adrenaline. In a matter of seconds, the body is transformed. To prepare for exertion, blood pressure and heart rate skyrocket; the liver pours out glucose and calls up fat reserves to be processed into triglycerides for energy; the circulatory system diverts blood from nonessential functions, such as digestion, to the brain and muscles. This is precisely what you need if your goal is to survive the next 10 minutes.

Civilization, by contrast, gives you the opportunity to experience an adrenaline rush at every traffic light. And--since all you're doing is sitting in your car--the elaborate preparations your body makes are wasted. Worse than wasted: every heartbeat at elevated blood

pressure takes its toll on the arteries. The excess fats and glucose don't get metabolized right away, so they stay in the bloodstream. The fats contribute to the plaques that form inside blood vessels, which can lead to heart disease or strokes; high levels of glucose are a step in the direction of diabetes. "If you mobilize in the first place for a nonsense psychological stressor," says Robert Sapolsky of Stanford, a leading authority on stress, "by definition your defense becomes more damaging than the imaginary challenge."

The second phase to the stress reaction kicks in five to 10 minutes later. This "hypothalamic-pituitary-adrenocortical axis" (HPA) seems more closely associated with emotional and intellectual stress. Researchers have many clever ways of producing intellectual stress, such as asking subjects to name the color of ink a word is written in (blue) when the word itself spells out the name of a different color (red). The HPA axis originates in the hypothalamus, in the middle of the base of the brain. The hypothalamus signals the pituitary to produce a substance called ACTH, which stimulates the adrenal cortex to produce a set of hormones known as glucocorticoids: cortisone, cortisol and corticosterone.

The action of these is complex, because hormones almost always work as part of a loop of positive and negative feedbacks. Glucocorticoids seem to stimulate the hippocampus, a part of the brain vital to memory and learning. But an excess of these hormones can actually be toxic to the hippocampus. People with above-average glucocorticoid levels--including those with depression and post-traumatic-stress syndrome--tend to have impaired memory and cognition. Their hippocampi may actually appear shrunken in an MRI scan. Glucocorticoids also suppress parts of the immune system. Researchers still don't understand why the body should suppress immunity during times of stress--if anything, the opposite would seem to make sense. But the negative effects are clear: chronic stress leaves one more vulnerable to infections.

And, amazingly enough, stress can even change the shape of your body. Since the stress reaction involves mobilizing the body's fat reserves for energy, Peeke says, it makes sense to store that fat near the liver, which processes it so it can be metabolized in the muscles. Sure enough, fat cells in the abdomen appear to be especially sensitive to glucocorticoids, and people with a high concentration of those hormones tend to accumulate fat around their middles--a potbelly--even if the rest of their bodies are thin. Researchers think that waist-hip ratio, the relative circumference of those two body parts, could be a useful way to identify people at risk for stress-related disease.

But not everyone gets all of these diseases, or even any of them. People respond differently to the same objective stressors. Individuals' cortisol levels vary (in general, the older you are, the higher the concentration), and they go up by varying amounts in reaction to stress. But, surprisingly, that effect doesn't seem to follow a normal bell-shaped curve, like most physiological variables. Instead, some studies suggest, people fall into categories of "hot" or "cool" responders. A 1995 study subjected 20 men to five grueling days of mental arithmetic performed before an audience. Starting from about the same baseline--a cortisol concentration in saliva of seven to eight nanomoles per liter--one group, comprising seven men, shot up to an average of 29 in the first day; the rest went only to around 19. The first group, researchers reported, "view themselves as being less attractive than others, having less self-esteem, and being more often in a depressed mood." Not surprisingly, they also reported more health problems.

Catherine Stoney of Ohio State has also found significant differences between men and women. Women's blood pressure goes up less than men's in reaction to stress (although their response increases noticeably after menopause or hysterectomy, suggesting a buffering effect from estrogen). But women tend to react to a wider range of outside stressors than men, according to Ronald Kessler of Harvard, who asked 166 married couples to keep a daily stress diary for six weeks. Women feel stress more often, says Kessler, because they take a holistic view of everyday life. A

man may worry if someone in his immediate family is sick; his wife takes on the burdens of the whole neighborhood. "Men take care of one thing [at a time]," he says. "Women put the pieces together again."

Apart from gender, early childhood experiences seem to have a powerful influence on how people deal with stress. Children raised in orphanages or in neglectful homes may have elevated levels of glucocorticoids and "hot" responses to stress later in life. "We're finding," says Frank Treiber of the Medical College of Georgia, "that if you come from a family that's somewhat chaotic, unstable, not cohesive, harboring grudges, very early on, it's associated later with greater blood-pressure reactivity to various types of stress." The brains of children up to around the age of 8 are still developing in response to the environment; cells literally live or die as experiences impinge on it. "The early brain can become hard-wired to deal with high fear states," says Dr. Jay Giedd of the National Institutes of Health. "Its normal state will be to have a lot of adrenaline flowing. When these children become adults they'll feel empty or bored if they're not on edge." Contrariwise, children raised in secure, loving homes learn to modulate the stress reaction, according to Megan Gunnar of the University of Minnesota. Newborns typically show a cortisol spike under the stress of circumcision. But as early as three months, well-cared-for babies can suffer discomfort without evoking a stress response; they'll cry when they get a physical exam, but their stress hormones don't go up commensurately. "Children who are in secure, emotionally supportive relationships are buffered to everyday stressors," she says.

Many authorities think childhood stress is on the rise. Dr. Barbara Howard, a pediatrician at Johns Hopkins, says a quarter of her patients are there for stress-related problems, and the proportion has been rising. "They'll come in with abdominal pain, urinary frequency, headaches... a whole variety of complaints which could be mistaken for medical problems and often are." Parents are frequently wrong about the sources of stress in their children's lives, according to surveys by Georgia Witkin of Mount Sinai

Medical School; they think children worry most about friendships and popularity, but they're actually fretting about the grown-ups. "The biggest concern," she says, "was that the parents are going to be sick, or angry, or they're going to divorce." And "often and somewhat surprisingly," says Giedd, "children have very global worries"--wars, environmental issues and crime, the same things adults worry about.

Which raises the question no researcher dares answer: is increasing stress an inevitable hazard of modern life? In many of the ways that count, Kessler muses, life was more stressful 200 years ago, when children routinely died before reaching adulthood. But life was simpler then, too, he thinks, before "anxiety became a core theme in our lives." People knew their place in society and lived with the support of extended families, tribes and villages. What is certain is that people came into the world then, as they do now, prepared by millions of years of evolution for dangers long gone from our lives. The challenge we face is to master not the threats themselves, but our all-too-human responses to them.

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