The Response to Stress

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What do we mean when we say we are "stressed out"? We may just be having a bad day, or feeling pressured by too many things to do and too little time to do them. Or we may have had a fight with a friend or family member. Or our job may be getting to us - feeling that it is just a rat race without a purpose, or feeling too much pressure and a lack of support and camaraderie. In any case, we are "bummed out" and "frazzled" and tend to think about how we feel at the moment and how to make it better right away. Rarely do we give much thought to the longer time frame and how our body is handling or not handling the pressure. Yet, it is the longer time frame of months and even years that is important for understanding the bad side of stress.

Stress activates adaptive responses. The body marshals its forces to confront a threat and, generally, does a good job of protecting us in the short run. So why can stress also be so bad for our bodies and brains?

Stress can prematurely age us and leave us chronically fatigued or depressed. When exposure to stress -- whether from a traumatic event to just the daily hassle of rush hour traffic or too much email -- disrupts the body's internal balance ("**homeostasis**"), it can go one of three general ways: the body can regain its normal equilibrium once the stress has passed or it can become stuck in an over- or under-aroused state. How a person copes with stress -- by reaching for a beer or cigarette as opposed to heading to the gym -- also plays a big role in the impact stress will have on our bodies.

How the Body Handles Acute Stress

When the body is challenged by almost anything that happens to us, from getting out of bed in the morning or running up a flight of stairs or having to stand up and give a talk, the brain activates the autonomic nervous system (ANS), the involuntary system of nerves which controls and stimulates the output of two hormones, cortisol from the adrenal cortex and adrenalin from the adrenal medulla. These two hormones and the activity of the ANS help us cope: the ANS and the adrenalin keep us alert by increasing our heart rate and blood pressure and quickly mobilizing energy reserves. In contrast, cortisol works more slowly, helps replenish energy supplies and, at the same time, helps us to remember important things. For example, cortisol readies our immune system to handle any threat -- bacterial/viral or injury.

Another aspect of cortisol action is called "containment." Many physiological systems are pitted against one another so that neither system can get out of control. The initial, first line response to many noxious or pathogenic agents is normally "contained" by circulating levels of cortisol. This is why we take corticoids for an inflammation or skin irritation. Cortisol also contains acquired immune responses, and this is particularly useful when those responses are harmful, such as in an allergy or an autoimmune disorder.

All of these adaptive responses are described by the term "allostasis" which means "maintaining stability, or homeostasis, through change."[1] The body actively copes with a challenge by expending energy and attempting to put things right. Most of the time it succeeds but the real problems arise when the systems involved in allostasis don't shut off when not needed or don't become active when they are needed.

Chronic Stress Response - Too Much of a Good Thing!
The way our body works presents us with a paradox: what can protect can also damage. This is called "allostatic load." It's the price the body has to pay for either doing its job less efficiently or simply being overwhelmed by too many challenges.[1]

For our metabolism, the over activity of the ANS and increased cortisol secretion produce elevated levels of sugar in the blood ("**hyperglycemia**"). As little as a week of inadequate sleep, say 75% of normal, can raise evening levels of blood sugar. If prolonged, what can result is a rise of insulin, the hormone manufactured by the pancreas to control sugar metabolism. If this situation goes on for a long time, continued hyperactivity of the ANS and elevated cortisol will lead the body down the path to type 2 diabetes. Elevated levels of cortisol, as in depressive illness, are also linked to gradual demineralization of bone.

For the cardiovascular system, the elevation of ANS activity, combined with hyperglycemia and too much insulin ("**hyperinsulinemia**") promote both hypertension and harmful metabolic conditions, as blood cholesterol rises and HDL, the so-called good cholesterol drops. This one-two punch accelerates hardening of the arteries ("**arteriosclerosis**"). Blood pressure surges seem particularly important. Among monkeys living in social hierarchies, the dominant males show accelerated atherosclerosis when the hierarchy is unstable and they have to continuously fight for their position. Treating these animals with beta-blockers, pharmaceuticals used to control blood pressure, prevented the increased atherosclerosis.

While acute stress actually improves our brain's attention and increases our capacity to store important and life-protecting information, for example, a source of danger, chronic stress dampens our ability to keep track of information and places. Chronic stress does this by impairing excitability of nerve cells and by promoting atrophy of nerve cells in the hippocampus, a region of the brain that is important for spatial and verbal memory.

For the immune system, which is controlled by the nervous system and by circulating hormones, chronic stress suppresses the ability of the immune system to do its job. This, once again, is in contrast to acute stress. Acute stress actually helps the immune system handle a pathogen by causing immune cells to move out of the bloodstream and into tissues where they are needed. Chronic stress, however, impairs not only the ability of the immune system to relocate immune cells but also the ability of those cells to do their job of recognizing and responding to the pathogenic agent.

Too Little of a Good Thing
But what happens when the body cannot mount an adequate response to an acute stress? Clearly, many of the good things that stress hormones do will not occur, like enhancing memory, replenishing energy reserves or moving immune cells to where they are needed. One other consequence, seen most clearly in the immune system, is that systems that are normally "contained" by cortisol become hyperactive. In the immune system, we find inflammatory agents (cytokines) and self-generated responses ("**autoimmune**") are no longer contained by circulating cortisol. As a result, disorders like arthritis and autoimmune diseases, for example, lupus, become worse. One treatment for such disorders, as we will discuss later on, is to treat the patient with cortisone or another glucocorticoid steroid.

How Our Behavior Can Help or Hurt Us
Besides regulating the endocrine system and the ANS and exerting a powerful influence on the immune system, the brain is the master organ for our behavior. And our behavior can help us or

hurt us in various ways. The most obvious way is to get us out of danger by flight or conciliation or to increase danger by confrontation or by risk-taking behaviors like driving recklessly. Another role of behavior is via health-damaging activities, e.g., smoking, drinking or eating too much of the wrong things, or health promoting behaviors such as exercise and eating a healthful diet. In other words, when we are under stress, it's important whether we reach for the bag of potato chips or go for a swim or a jog. Eating a rich diet and drinking alcohol feed into the allostatic load -- they increase the levels of these stress mediators and, thus, make hypertension and insulin resistance, among other consequences, more likely.

What We Can Do to Better Handle Stress

Individuals may differ in their health and well being because they differ in behavioral and neuroendocrine adaptive mechanisms, that is, the ways in which their hormone and nervous systems react. You might, compared to a friend, have higher or lower allostatic load, not only because you are subjected to different degrees of life stressors but also because you are "wired" differently and have had different life experiences that make you react in different ways.

Whatever the cause may be, protecting your body against over-exposure to stress hormones is as important to the body as the ability to mount an adequate allostatic response in the first place. Either type of imbalance in allostasis qualifies under the definition of "allostatic load." People with long-term histories of persistent and relatively small elevations or deficiencies in stress hormone levels may show accelerated progress toward pathophysiology and disease. In the case of excess hormone production, these disorders include atherosclerosis, obesity, type II diabetes and cognitive impairment. For relative hormone insufficiency, the pathophysiology includes autoimmune and inflammatory disorders, chronic pain and chronic fatigue.

In dealing with the type of allostatic load involving hormone over-production, it is important to use behavioral coping skills to control over-production of stress hormones in challenging situations. This includes seeking social support, counting to ten and resisting an intemperate reaction or simply withdrawing from a situation rather than risking a destructive confrontation. Behavioral coping also includes engaging in health promoting behaviors, such as regular moderate exercise and a healthy diet with moderate food intake and controlled alcohol intake. It is also important to learn to see situations as a challenge and an opportunity, rather than as disasters about to happen. If this sounds like an admonition to "positive thinking" it is exactly that. These types of behaviors represent a first line of defense against the development of allostatic load.

In the case of relative hormone deficiency, there are experimental programs to treat with low dose glucocorticoids in the case of chronic fatigue syndrome and chronic pain but these have had mixed results.[2] Admittedly, the medical community is still not certain how to treat these conditions.

How Your Doctor Can Help

Although allostatic load is a subtle phenomenon, your doctor needs to take it into account in diagnosis and treatment. A doctor can help you reduce allostatic load by encouraging you to learn behavioral coping skills that will enable you to recognize your limitations and teach you to relax. These are simple steps every doctor can provide even without the results of further research. Your doctor can also assess other areas of your health and remind you about the interactions of high fat diet and stress in atherosclerosis, the role of risky behaviors such as smoking in cardiovascular disease and cancer, and the beneficial effects of exercise. However, there are limits to what such advice can accomplish. While your doctor may point these and

other matters out to you, your decision to follow the advice and your ability to change behavior patterns[3,4] are, of course, critical.

Clearly, doctors of all types are involved in providing advice, counseling and/or psychotherapy aimed at helping patients deal in a more healthy way with the many stressors of life. Interestingly, different psychotherapeutic approaches might address more efficient and less costly allostasis in different ways. For example, cognitive therapy focuses on better labeling of the stimuli in the environment so that the same stimuli are subsequently interpreted in a less threatening, arousing way. On the other hand, behavioral or exposure therapy focuses on keeping the individual in a threatening environment long enough to allow the neuroendocrine and autonomic systems to handle the situation. For example, a person with a fear of flying might be treated with air travel simulations until their body learns to "cope" with the fear. Whatever you do, it is important that the right psychotherapeutic" strategy appropriate for you and your "nervous system" be selected.

Does Everybody Suffer from Stress?

The biggest problem with the frequent patient complaint of the 90s, "I'm stressed out," is that it is so general. The father of stress research, Hans Selye, writes in his autobiography[5] that he was first struck by how people with many different types of illness all had some common symptoms best described as "feeling sick." Selye believed that stress caused "flight or fright." Now, we even know that stress can sometimes cause us problems by making us react too little. As noted above, under arousal (insufficient allostatic response) to a stressor is potentially as damaging to the body as prolonged arousal. So, today, we now understand that being "stressed out" or being "sick and tired" are actually the symptoms of a mismatch -- your body has not reacted correctly to the challenge or threat it faced. Unfortunately, researchers haven't figured out how much of an allostatic response is necessary or harmful.

A classic example is fever. It's not clear whether a doctor should treat it with medicine or let it run its course.[6] Fever is often a good and natural response ("adaptive") to an acute infectious agent but the person with a fever must pay a significant price in "feeling sick." It now appears that the treatment of a fever might actually delay recovery from an infectious process. Similar questions are raised about the use of anti-inflammatory and whether they might sometimes interrupt a healing process.

So, treating an allostatic response might be hazardous. Interestingly, some people with infectious episodes go on to develop the Chronic Fatigue Syndrome (CFS), which is often characterized by intermittent feverishness and malaise like that occurring with an infection, even though the person has no infection. It appears that this is a disorder where an inappropriate "allostatic" response is being made and this includes an insufficiency of the production of stress mediators like cortisol. Treatments will likely center on how to make the allostatic responses mounted by the CFS patient more appropriate. As we have already noted, this may include giving low dose cortisol treatment to supplement what the body produces.

Another situation often confronting doctors is whether or not to treat a patient for the symptoms arising in the wake of the loss of a loved one. Bereavement is characterized by many, but clearly not all, of the symptoms of depression, such as depressed mood, tearfulness and changes in sleep and appetite.[7] Yet, many regard bereavement to be a restorative, healing and even necessary part of the process of losing a loved one. However, some bereaved people experience symptoms of such severity and length that treatment for depression is pursued.

Developing clear and useful standards for differentiating healing from unhealthy bereavement is

an ongoing but difficult job and a clear example of the types of judgments facing the doctor who is going to treat the mismatches of challenge and allostatic response.

In the future, we will need to develop better detectors for environmental stressors (infectious, interpersonal, etc.), better detectors for allostatic response and better ways of determining whether a response is turned on too much or too little or is of too long or too short a duration. This allostatic framework, however, will help guide you and your doctor as you together decide whether you're sick or stressed out.

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