Stress: Part I
The physiology of stress

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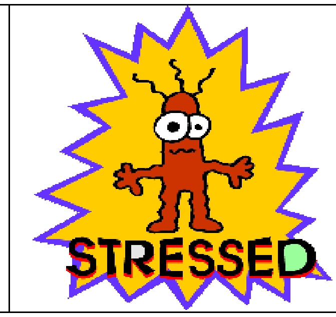

In the upcoming series of articles, we tackle the enormous topic of stress. It is generally agreed by the scientific community that stress is not what happens to someone. Stress is how a person reacts to stressors. Stress affects everyone differently. Stressors can be positive -- exciting things like graduating, getting married, or going on vacation -- or stressors can be negative things, like worrying about the bills, breaking a leg, or dealing with traffic on your daily commute.[1, 2] These stressors can be can be sudden, one-time occurrences or repeated, leading to a chronic problem. Stress can be a result of either physical or psychological factors. We often get stressed by expecting or imagining disasters that do not and may never occur.[2] The body's response to stress is comprehensive and complex, and it affects the operation of many systems.

When Repetitive Stress Injury is discussed and/or diagnosed, typically only the physical effects of repeated abuses exerted on the body from the outside are considered. Unfortunately this is not the whole problem. In this article, we address repeated stress in the physical and psychological traumas of everyday activities, our emotional reaction to the traumas, the hormonal responses of the body to the emotions, and the changes that occur to the body as the result of repeated exposure to these factors. We believe it is best to begin with a solid understanding of the body's response and what stress does to the body in the short and long term. The rest of the articles in this series will address the psychological profiles of people who experience different types of stress, which profiles are the most harmful, and what can be done to turn things around. Finally, we will supply a "menu" of tips gleaned from popular and scientific literature that we hope will help you decide what is right for your life.

An interesting history of stress research:
Since the days of René Descartes, the seventeenth-century mathematician, Western science has followed the doctrine that the mind and body are separate. Today, thanks to the ineptness of an endocrinologist, Hans Selye, we are now well aware that emotions and the mind play a critical role in our physiological responses, though many doctors still sadly practice medicine as if they were separate.[2, 3, 4]

In the 1930s, Selye was an assistant professor attempting to do some research on rats to determine the effects of an ovarian extract. He would try to inject the rats, but would end up dropping them on the floor, chasing them around the room, and finally injecting them with the extract.[2] At the end of several months of this, Selye found that the rats had peptic ulcers, greatly enlarged adrenal glands (the source of two important stress hormones), and shrunken immune tissues. As in all good research, he ran a control group and injected rats with just saline solution. He was surprised to find the same symptoms. Clearly, the physical problems were not the result of the ovarian extract. Selye thought about his treatment of the rats and reasoned that perhaps there were changes in the rats' bodies as a result of the traumas they had to suffer under his handling. To test this during the winter, he put some on the roof of the research building and some in the boiler room; some were forced to exercise, and some underwent surgical procedures. All of the rats developed peptic ulcers, adrenal enlargement, and atrophy of the immune tissues.[2] He borrowed the engineering term – *stress* – to describe the phenomenon. He made two observations:

- The body has a set of similar responses to a broad array of stressors.
- Under certain conditions, the stressors will make you sick

In fact, this general type of phenomenon had been identified 10 years earlier by a Harvard University physiologist, Walter Cannon, as the "fight or flight response".[2, 3] Cannon theorized that mammals have a physical ability to react to stress that evolved as a survival mechanism. When faced with stressful situations, our bodies release hormones - epinephrine (adrenaline) and norepinephrine (noradrenaline) - that elevate the heart rate and increase blood flow to the muscles, gearing our bodies either to do battle with an opponent or to flee.[3]

Today our knowledge of the stress response has been refined further through the advancements made in technology and science, but the basis of our understanding still confirms the theories of these two "fathers of stress".

The physiology of stress

As noted above, the body has a similar set of responses to a broad array of stressors.[2] These responses include:[1,2, 5]

1. Rapid mobilization of energy from storage. Glucose, simple proteins and fats pour out of fat cells, liver, and muscles.
2. Increased heart rate, blood pressure, and breathing to speed up the transport of nutrients and oxygen.
3. Inhibited growth and decreased sex drive. Females are less likely to ovulate or to carry pregnancies to term; males secrete less testosterone and have trouble with erections.
4. Halted digestion. The large intestine is stimulated to release previously digested food to reduce body weight.
5. Inhibited immunity to save the body's energy for the crisis at hand.
6. Diminished perception of pain.
7. Improved cognitive and sensory skills. Memory improves, except in the case of prolonged or extreme stress.

All of these responses are meant to be short-term in order to mobilize the body for action. They are short-sighted and inefficient, but they are important in a physical crisis situation.[2] They evolved over the millennium when threats tended to be predators chasing us to eat us. To a great extent, these physiological responses are completely useless in the context of giving a speech, hearing disturbing news on TV, or handling spiraling health care costs. These types of stressors have arisen only within the past few centuries; therefore, we have not had enough time to evolve biologically to cope in new ways. "Modern" stressors are no longer short-term; they have become chronic. The risk of disease has increased as a result.[2] So, it is up to us to understand what is happening in our bodies when we experience stress and to learn to deal with it in a way that causes as little damage as possible.

Hormones of the Stress Response

The autonomic nervous system controls bodily functions which we are largely unaware of and do not consciously control. The part of the autonomic nervous system that is activated during emergencies is the *sympathetic nervous system*, which speeds up systems needed for survival.[1,2] The other part of the autonomic nervous system, the *parasympathetic nervous system*, plays an opposing role. It mediates passive activities and promotes growth and energy storage. Parts of this system are also called into play during stress to slow down systems not required for survival.[1,2]

When something stressful happens or you think a stressful thought, many hormones are released by the brain, nervous system, and other organs:

- The base of the brain, the hypothalamus, secretes an array of hormones into the blood, mainly corticotropin releasing factor, which triggers the pituitary to release the hormone corticotropin (ACTH).[2] ACTH in the bloodstream triggers the release of glucocortoids by the adrenal gland.
- The sympathetic nervous system releases epinephrine (adrenaline), and norepinephrine (noradrenaline) into the bloodstream[2]
- The pancreas releases a hormone called glucagon, which raises the circulating levels of glucose in the blood[2]
- The pituitary releases prolactin, suppressing reproductive systems and vasopressin, the anti-diuretic hormone
- Both the brain and the pituitary release morphine-like substances called endorphins and enkephalins which limit pain perception.[1,2]

Epinephrine and glucocortoids appear to act in similar ways, however epinephrine acts within seconds, while glucocortoids are slower-acting, backing up the epinephrine for minutes or hours.[2] Together, epinephrine, norepinephrine, and the glucocortoids account for a large portion of what happens in the body during stress.[2]

At the same time, the secretions of the reproductive hormones (estrogen, progesterone, and testosterone) and the growth hormones are inhibited during stress to conserve energy for the imminent fight or flight. The secretion of insulin is also inhibited, which normally tells the body to store energy. [2]

The pattern of the body's response to stress is not consistent. Massive physical stressors result in hormonal changes, with the glucocortoid and epinephrine/norepinephrine response being the most reliable.[2] More subtle stressors result in a variety of responses. For example, anxiety and vigilance types of stress may result in the release of epinephrine and norepinephrine, while depression and giving-up types of stress may result in the release of glucocortoids.

Depending on the anticipated type of stress, the psychological context of the stressors causes the release of these hormones and other chemicals, collectively called *peptides*.[2] Peptides are strings of amino acids that are the means of communication within and between all parts of the body.[6] They are detected by receptors in other parts of the body, which results in changes to those body parts. [6] The peptides and their receptors are considered the biochemical correlates of emotions. [6]

Stress and Heart/Cardiovascular Disease

The stress response is most maladaptive in the heart and cardiovascular system because it causes the whole system to work harder. With repeated stress, the heart and blood vessels wear out.[2] This occurs most often where arteries branch, due to turbulence of the blood at branching.[2] The smooth inner lining of the vessel begins to tear, scar, and pit. Fatty acids and glucose in the blood, mobilized by the stress response, begin to work their way under the lining of the blood vessel, stick there, and cause thickening.[2] In addition, epinephrine causes fatty nutrients to form and makes the blood thicker and more likely to clot.[2] The blood vessels start to clog up and blood flow decreases. This result is called atherosclerosis, which is a demonstrated result of chronic stress in several species, including humans.[2]

Once the cardiovascular system is damaged, it is extremely sensitive to stressors, either physical or psychological. Stress can cause the sympathetic nervous system to send two symmetrical signals to the heart that cause it to misfire.[2] Sudden joy or grief has a similar effect on the cardiovascular system.[2] This is not true for the reproductive system, the growth system, or the immune system.[2]

A recent review of studies published between 1970 and 2004 found convincing proof that extreme physical exertion (particularly in individuals not accustomed to exercise), psychological stress, anger, and over-excitement can lead to chest pain, heart attack, and sudden cardiac death in those at risk for heart disease.[7] These studies differ from previous ones that assess risk factors for developing cardiovascular disease such as inactivity, cigarette smoking, chronic stress, and anger. The new studies identify sudden, acute changes that appear to precipitate heart attacks in an already susceptible population of patients.[7]

Individual differences account for much of the risk of cardiovascular disease:[2, 8]

1. An already damaged cardiovascular system.
2. Genetic factors influencing the mechanics of the system such as the elasticity of blood vessels and the number of norepinephrine receptors.
3. Smoking, high blood pressure, or high triglyceride levels.
4. Personality (specifically Type A, hostile or angry).

Scare tactics have little effect on changing old habits, so it is best to discuss the choices that can be made to promote wellness and health. Research has shown that making modifications to lifestyle, including exercise and diet, can actually cause arteries to become less blocked! This is something that was previously not believed to be possible.[4] Heart bypass and angioplasty surgeries, in addition to being horrendously expensive, have not proven to be effective in increasing life expectancy in most cases. However, changes in exercise and diet have reversed the damage to the cardiovascular system, and have improved health and wellbeing.[4] Coping with both lifestyle and emotional stress can reduce the risk of cardiovascular disease, especially for the Type A personality.[4, 2] This will be discussed in our third article.

Stress and Diabetes

Type 2 (adult-onset) diabetes is the result of the body's response to inactivity and a surplus of fat. It is a common problem in Western populations. There is no increased risk of this disease in non-westernized populations. With diabetes, the body becomes resistant to insulin, the hormone that tells the body to convert circulating fats, proteins, and sugar into fat and protein. If enough fat is stored and the fat cells are full, they become less responsive to the insulin. The cells lose their specialized receptors for insulin. There is too much circulating glucose and fatty acid that damage the kidneys, blood vessels, and eyes. The stress response causes even more glucose and fatty acids to be mobilized in the bloodstream. It blocks insulin production and it promotes insulin resistance. Chronic stress can cause atherosclerosis in someone who is already insulin resistant or borderline diabetic due to the increase of circulating fatty acids and glucose.[2]

Type 1 (juvenile) diabetes is insulin-dependent diabetes.[2] The immune system attacks the cells of the pancreas that secrete insulin, so the person has a reduced capacity to produce insulin. With reduced insulin, there is little capacity to store excess glucose and fatty acids, so cells starve while there is excess circulating fatty acids and glucose in the bloodstream.[2] These clog the kidneys, form atherosclerosis in the blood vessels, and link proteins in the eyes, causing cataracts.[2] Stress aggravates Type 1 diabetes.

15% of people over 65 in the U.S. have insulin-resistant diabetes. The disease more than doubles mortality and nearly triples the rate of heart disease in men. It is the leading cause of blindness and the 7th leading cause of death.[2]

Even without diabetes, stress causes mobilization of energy sources. Shuttling nutrients in and out of the bloodstream costs energy, so if you are stressed frequently, you will tire more easily and experience regular fatigue.[2]

Stress and the Digestive System

The digestive system quickly shuts down during stress.[2] The first noticeable sign is a lack of saliva and dry mouth. Chronic stress results in diseases of the digestive system.

Ulcers are still not well understood, but the discovery of the bacteria *Helicobacter pylori* has lead to the understanding that this bacteria is a predisposing factor in ulcer formation.[2] However, since most people have this bacteria in their digestive systems, it cannot account for all ulcers.[2] Approximately 10% of the people infected with the bacteria develop ulcers.[2] 15% of duodenal ulcers form in people with no Helicobacter infection.[2] So, there must be at least two factors acting together, such as non steroidal anti inflammatories (eg. Aspirin), a genetic tendency to secrete too much acid or to secrete insufficient mucus to protect the stomach lining from acid, or ….stress.[2] Many studies have shown that people who are anxious, depressed, or undergoing severe life stressors are more likely to experience duodenal ulcers.[2] It has been shown that a little stress with tons of bacteria OR lots of stress with just a little bacteria will cause an ulcer.[2]

The link between stress and irritable bowel syndrome has not been successfully proven because it is very difficult to study and document. However, it is fairly well recognized that chronic stress worsens existing cases of gastrointestinal problems including colitis for some people.[2]

The effect of stress on appetite is still being researched, but we do know that two opposing systems are activated when a stressful event occurs. Corticotropin and Corticotropin releasing factor, hormones released in the stress response, suppress appetite for the short term. Under longer episodes of stress, these hormones are probably released for a longer period of time. Glucocortoids are also released. They are slower acting and stimulate the appetite.[2] Presumably this system works for the immediate physical threats requiring the fight-or-flight response (i.e., lose appetite at first but then get hungry to replenish the energy expended once the event has passed).[2] The different parts of the system work together, one for the immediate response and one for the recovery.

Stress and Cancer

There is no conclusive evidence that stress either leads to a greater incidence of cancer or that existing cancers progress more rapidly. Some sources claim a higher risk of cancer with stress [5], but scientific research with humans has not proven this.[11, 12, 13] There appears to be a link between personality type and increased cancer risk, but lifestyle variables were not ruled out in this research.[2] Conforming, compliant people are somewhat more prone to cancer, but they may also have a higher incidence of smoking, drinking or fat consumption which may account for this increase in cancer risk.[2] One study has found that severe life stressors cause a small, but significant increase in breast cancer in women, though medical experts still do not agree whether stress alone contributes to the incidence of cancer development since the issue is generally confounded with other complex lifestyle and genetic variables.[14]

The most harmful theories about cancer are those professing that with enough courage, spirit, and love, cancer can be prevented or cured.[2] In the case of childhood cancer, it is implied that the parents are at fault because they are not providing a sufficiently nurturing environment. Everything bad in human health is not caused by stress and it is negligent to imply that we can cure ourselves of cancer by thinking healthy thoughts.[2]

Stress-induced pain relief

The body synthesizes three different classes of opoid compounds: enkephalins, dynorphins, and endorphins.[2] Release of these compounds in stressful situations is shown to occur on the battlefield, in sports, and in everyday exercise programs.[2] After about 30 minutes of exercise, endorphins are released, masking sensations of pain, causing a “runner’s high”. Many other types of stressors including surgery, low blood sugar, exposure to cold and childbirth, produce similar effects. [2,15] From an adaptation standpoint this makes sense when one must run from the enemy or fight despite injury. With prolonged exposure to stress, however, the body’s supply of opoids runs out and the sensation of pain returns. There appears to be no stress-related disease that results from excess opoid release.[2]

Stress and Memory

Short-term stressors of mild to moderate severity enhance thinking, while enormous or prolonged exposure to stress is disruptive to cognition.[2] With short-term stress, the sympathetic nervous system kicks into gear, pouring epinephrine and norepinephrine into the bloodstream. Glucose is dumped into the bloodstream, and there is increased blood flow to the brain.[2] Glucocortoids, released by the adrenal glands adjacent to the kidneys, are mildly elevated. The hippocampus, the part of the brain responsible for placing and retrieving memories in the cortex, is extremely sensitive to glucocortoid levels. [2,15] With increased glucocortoids available during stress, memories are retrieved more quickly. Levels of glucocortoids vary with the time of day, generally highest in the morning at around 6-8 am and lowest around midnight.[15] Another part of the brain, the amygdala, also influences memory storage and recollection by releasing hormones.[16] While the hippocampus mediates conscious memories, the amygdala mediates unconscious memories and the way your body responds based on past experiences.[17]

In the case of big stressors or long-term stress, an enormous amount of sympathetic arousal disrupts the potential of the hippocampus.[2] After about 30 minutes of stress and prolonged exposure to glucocortoids, the hippocampus neurons take up about 25% less glucose, so the energy supply is decreased.[2] Glucocortoids actually begin to damage neurons in the hippocampus, reducing its volume by up to 14%.[2,16,17] The end result is that under high or prolonged stress, memory and concentration are impaired.[2] However, at the end of the stressful period, it appears that neurons can regenerate their connections.[2]

Victims of abuse have been found to have 5% reduction in volume of the hippocampus. People with smaller hippocampi are more likely to suffer post-traumatic stress disorder.[16] In addition, it has been shown that memory performance of both older adults and young adults can be significantly altered by manipulating glucocortoid levels.[17] Overall, it can be concluded that experiences cause a chemical change within the brain which alter the structure of the hippocampus.[16]

Current implications in research indicate that high glucocortoid levels increase damage if another neurological insult is added, such as Alzheimer’s, AIDS, epileptic seizure, or stroke.[2] Unfortunately, doctors often prescribe synthetic glucocortoids to stroke patients in an attempt to reduce inflammation, and they are often prescribed to AIDS patients to combat various aspects of the disease. But, the result may well be greater damage to the hippocampus and increased likelihood of dementia and memory loss.[2]

Stress and Aging

As people and other organisms age, their epinephrine, norepinephrine, and glucocortoid levels rise in the normal resting state when there are no stressors present.[2] When there is a stressor, levels rise higher than they do in younger people, but the body is less responsive to them. After the stressor is gone, the levels of these hormones do not return quickly to pre-stress levels. Therefore, it takes older people and organisms longer to recover from stress.[2]

Glucocortoids cause aging of many of the body's systems. As we get older, our ability to regulate glucocortoid levels in our bloodstream degenerates.[2] The hippocampus loses a considerable number of neurons which affects the brain's ability to control glucocortoids. Increased glucocortoid levels damage the neurons in the hippocampus which, in turn, impedes the feedback for controlling glucocortoid levels. One theory as to why this happens is that perhaps memories actually serve to slow us down.[16] Reliance on the amygdala to signal the brain that there is danger and a need for survival tactics, without interference from the hippocampus, may be more adaptive from a flight-or-flight standpoint.[16]

Fortunately, many humans and other organisms age successfully in a way that spares them the cascade of hippocampal destruction.[2] Not enough is known yet to understand how this works in humans, but it appears possible that a lifetime of severe stress or heavy long-term use of synthetic glucocortoids to treat some disease may accelerate aspects of this cascade.[2]

This concludes our overview of how stress affects various systems of the body. In the next article we will discuss the psychological and social factors that modulate the stress response of the body. In the final article we will share strategies for managing and coping with stress.

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This article and all of our articles are intended for your information and education. We are not experts in the diagnosis and treatment of specific medical or mental problems. When dealing with a severe problem, please consult with a healthcare or mental health professional and research the alternatives available for your particular diagnosis prior to embarking on a treatment plan. You are ultimately responsible for your own health and treatment!

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REFERENCES:

1. *Stress & Anxiety* [videorecording] / Time Life Medical; produced in association with Sonalysts Studios. New York, NY; Patient Education Media, ©1996. ISBN 1575770180

2. Why Zebras Don't Get Ulcers, Sapolsky, R.M., ©1998 W.H.Freeman and Co., New York, ISBN 0-7167-3210-6.

3. The Relaxation Response, Benson, H., M.D., ©1975and 2000, William Morrow and Co., Inc., Quill/Harper Collins Publishers, Inc., New York, NY. ISBN 0-380-81595-8

4. Healing and the Mind, Bill Moyers. *Changing Life Habits*, interview with Dean Ornish. ©1993 Public Affairs Television, Inc. and David Grubin Productions, Inc. Doubleday, New York. ISBN 0-385-46870-9

5. The Joy of Stress, Hanson, P.G., M.D. ©1986, Peter G. Hanson, M.D., Andrews, McMeel & Parker, Kansas City, MO. ISBN 0-8362-2411-6

6. Healing and the Mind, Bill Moyers. *The Chemical Communicators*, interview with Candace Pert. ©1993 Public Affairs Television, Inc. and David Grubin Productions, Inc. Doubleday, New York. ISBN 0-385-46870-9

7. *Stress Can Be Heart Attack Trigger*, Stöppler, M.C.,M.D., ©2005, About, inc. http://stress.about.com/od/heartdisease/a/hearttriggers_p.html

8. Stress: Living and Working in a Changing World., Manning, Curtis, and McMillen. ©1999, George Manning, Kent Curtis, and Steve McMillen. Whole Person Associates, Inc., Duluth, MN. ISBN 1-17025-176-2

9. *Job Stress and High Blood Pressure: Is your your workplace stress putting you at risk?* Stöppler, M.C., MD. ©2005 About, Inc. http://stress.about.com/cs/workplacestress/a/aa090401.htm?terms=perceived+job+stress+blood+pressure

10. *Perceived job stress but not individual cardiovascular reactivity to stress is related to higher blood pressure at work.* Fauvel, J.P., Quelin, P., Ducher, M., Rakotomalala, H., Laville, M., Hypertension. 2001 Jul;38(1):71-5. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=11463762&dopt=Abstract

11. *Psychological Stress and Cancer*, National Cancer Institute, 3/9/1998, http://cis.nci.nih.gov/fact/3_17.htm

12. *Probing links between stress, cancer*. Azar, B, ©1999 American Psychological Association, APA Monitor Online, Vol 30(6), June 1999. http://www.apa.org/monitor/jun99/stress.html

13. *Stress and Uterine Cancer*, Stöppler, M.C.,M.D., , ©2005, About, Inc. http://stress.about.com/od/medicalconditions/a/endometrial_p.htm

14. *Can Stress Increase Breast Cancer Risk?*, Stöppler, M.C.,M.D., ©2005, About, Inc. http://stress.about.com/cs/womenshealth/a/aa040303a_p.htm

15. *Cortisol: The "Stress Hormone"*, Stöppler, M.C.,M.D., ©2005, About, inc. http://stress.about.com/cs/cortisol/a/aa012901.htm

16. *Determining the Intensity of a Memory*, Taverna, K., Jan, 2002. ©1994-2005, Serendipity. Center for Science in Society, Bryn Mawr College, 101 North Merion Ave., Bryn Mawr, PA 19010-2899. http://serendip.brynmawr.edu/bb/neuro/neuro98/202s98-paper3/Taverna3.html

17. Emotion, Memory, and the Brain: What the Lab Does and Why We Do It. LeDoux Laboratory, Center for Neural Science, New York University. http://www.cns.nyu.edu/home/ledoux/overview.html