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Robert M. Sapolsky

Why Zebras Don't Get Ulcers: Stress, Disease & Coping

Let's start with a short survey about all of your families' medical histories. How many of you have a family member with a history of heart disease? High blood pressure? Stroke? Ulcers?

Ok, now how many of you have a family member with a really bad, fulminating case of leprosy? No lepers??? How about dysentery? Does anyone have a family member with liver flukes the size of your fist? No hands there either!

These results are actually not surprising. The odds are that none of us in this room are worrying about smallpox or scarlet fever. Very few of us will get malaria during the rainy season. Very few of our mothers died in childbirth. No one in this room is malnourished. In all of these ways, we are completely unlike any animal that has lived before us on Earth. We are unlike our recent ancestors, and we are unlike the people in the developing world. Westerners have an amazing luxury in that our bodies spend eighty years going to hell on us. That's absolutely great! We will not be killed by a serious case of dengue fever when we're twenty years old.

A New Era of Disease

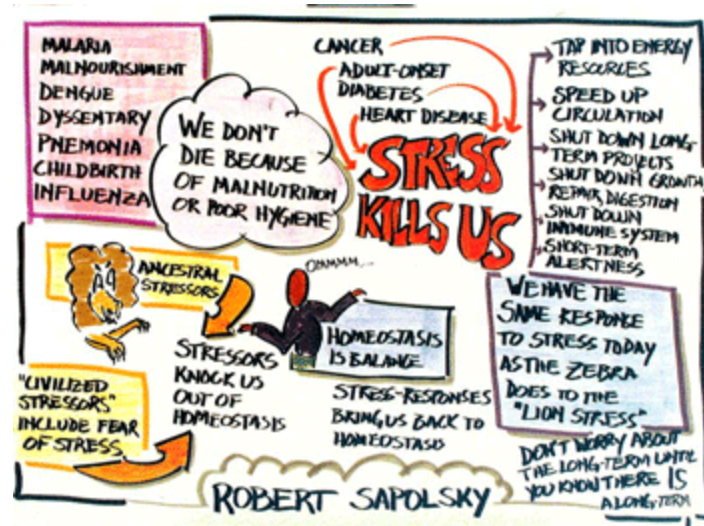
We are now facing a completely different realm of disease. With the exception of AIDS and TB, we do not worry about infectious diseases anymore. We don't worry about the diseases of poor nutrition and poor hygiene. It is a Westernized luxury to have our bodies slowly accumulate damage over many years. This is a very different way of getting sick.

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Around 1900, the leading causes of death in the United States were dysentery, TB, pneumonia. If you were a woman between the ages of 20 and 40, the single most risky thing you could do was to get pregnant - many women died during childbirth. The number one killer of Americans in 1900 was influenza - the flu! In 1918, the worst winter of World War I, you had a better chance of surviving if you were sent to war than if you caught the flu. There were eight million war deaths in WWI, and 25 million civilians died of the flu in the winter of 1918.

Today, no one under the age of 90 dies of the flu. Instead, we die of all sorts of mysterious diseases that have never existed before on this planet. These include cancer, heart disease, adult-onset diabetes, Alzheimer's - we are suddenly dealing with radically different ways of getting sick.

Ten thousand years ago, if you were a young hunter-gatherer who had just made a major medical mistake - you had just eaten a reed buck riddled with anthrax - then your medical outcome is absolutely clear. You have about 48 hours left to live.

Today, a young American will make a major medical mistake by eating a lot of saturated fat and red meat, but the medical outcome is totally unpredictable. This person might be dead by age fifty, or running marathons with she's 85. What makes the difference between the person who dies young and the person who lives? Some of the factors are very technical, like how well your liver handles cholesterol. But some of the factors are variables that we have never had to think about before in human history - like your psychological make-up, your social status, your society. This moves us into an entirely different realm of medicine.

The diseases that are going to kill us are caused by or made worse by

stress. Most of us in this room will drop dead of a stress-related disease someday so it probably makes sense for us to learn a little bit about it.

Homeostasis, Stressors and the Stress Response

Let's start with some definitions. Homeostasis is the state of balance for our bodies - the ideal body temperature, ideal level of glucose in our blood streams, etc. A stressor is anything in the outside world that moves our bodies out of homeostatic balance. If you are a zebra and a lion has just jumped out at you and torn open your stomach and your innards are dragging in the dirt and you really need to get away, this is an example of being out of homeostatic balance. Or, if you are a lion who is malnourished and you will not survive the night unless you can hunt down a meal, then you are out of homeostatic balance. Stressors are short-term crises that knock you out of homeostatic balance.

The stress-response is what you do to reestablish homeostatic balance.

These definitions are pretty simple for zebras, but these are a little more complicated for humans. Stressors are things that knock you out of homeostatic balance, but for humans, stressors also include those times when you think that you're about to get knocked out of homeostatic balance. It is quite advantageous for us to have a cerebral cortex that can see danger coming and stimulate an anticipatory stress-response. On the other hand, if you think that you are about to be knocked out of homeostatic balance on a regular basis when you're really not, then there are several ways to describe your state of mind - neurotic, anxious, paranoid, hostile, or profoundly human. A hippo, for example, has no way of seeing its retirement fund performance as a stressor.

For 99% of the beasts on this planet, stressful situations include about three minutes of screaming terror, after which the threat is over or you are over. We humans turn on the exact same stress-response thinking about 30-year mortgages, and the catch is that this response did not evolve to be turned on chronically. As a higher-order primate, we have developed the amazing capability to turn on the same stress response as a zebra or lion, only we turn it on with thought and emotion. If we turn on the stress-response chronically, we are going to get sick.

Here is an exercise you can do to prove that this is the way it works. When you get into bed tonight and you are feeling comfortable and relaxed, feel your heart beating nice and slowly. Then think to yourself the following thought: "You know, my heart is not going to beat forever." I will bet you that your heart speeds up at that point! You will not have just run up a flight of stairs or hauled a cow around the stockyard, yet you will have turned on a stress-response merely with thought.

The Discovery of the Stress Response

This is the key to understanding how we as a species are so vulnerable to stress-related diseases - we turn on the basic mammalian stress-response simply with thought. Why should our bodies turn on the same response as the bloody zebra or the starving lion in completely different circumstances? This is the question that Hans Selye, an Austrian physician wrestled with 70 years ago. He started this entire field of study.

Hans Selier was smart, creative, insightful and totally incompetent at handling laboratory rats. He was a young assistant professor at McGill University, looking for a research project that would make him famous. A biochemist down the hall had just isolated a hormone in the pancreas, so Selier decided to study what effects this hormone had on the body. He took a load of this hormone and started injecting rats with it. Apparently, he was very bad at handling the rats, and he spent months injecting them, dropping them, and chasing them with brooms. At the end of the study, he examined the rats and made an amazing discovery: they all had stomach ulcers!

Selier was euphoric. He had just discovered the effect that this pancreatic hormone on the body! Now at this point Selier decides to take a look at his control group as well. These were rats who were getting injected with saline rather than the pancreatic stuff, but they had been living in the same conditions as the other rats - getting injected and dropped and chased with the broom. It turned out that these rats had stomach ulcers too!

At this point, your average scientist gives up and goes to business school, but Selier stops to really think about this. These results clearly were not dependant on the pancreatic hormone. Selier recognized that the life these rats had been leading was not terribly pleasant, and he decided that these stomach ulcers were a non-specific response by the body to generalized unpleasantries. He then devised a series of experiments in which he systematically exposed rats to a variety of different unpleasantries - heat, cold, loud music, cats, etc. In every case, these rats developed stomach ulcers.

Selier had discovered the tip of the iceberg of stress-related disease. Selier took the obscure term "stress" from metallurgy which related to torsional strain, and applied it to living systems. He identified the stress-response system in animals which saves your life if it lasts very briefly, and makes you sick if it goes on for too long.

Everyone in physiology thought Selier was crazy. Physiology taught us that the body comes up with very specific solutions to very specific challenges - if you're hot, you don't shiver. Selier was arguing for a very general response from the body to a wide variety of stimuli - our bodies react the same way if we are the zebra, the lion, too hot, too cold, or on a blind date.

The Stress Response: Step by Step

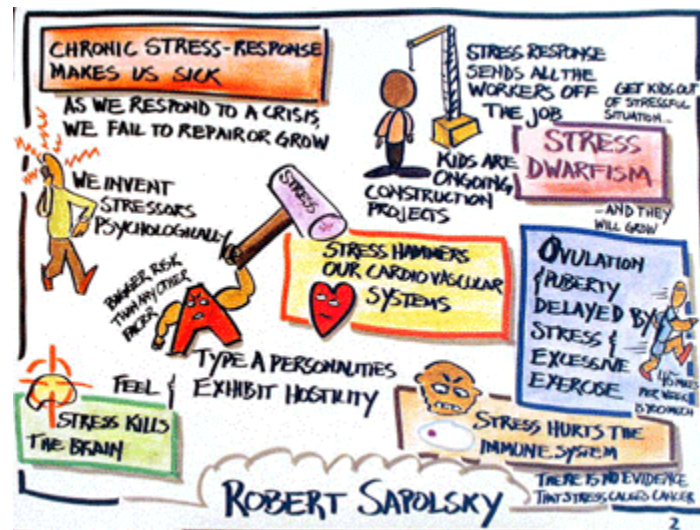
Why should the stress-response be turned on in the exact same way in all of these different circumstances? If you are going to survive a short term crisis of any kind, there are certain things that your body needs to do. Above all else, you need to mobilize as much energy into your bloodstream as you can. You don't need to worry about storing energy. You tap as deeply into "the bank" as you can - your liver and your fat cells - and you convert the stored energy into circulating glucose. Forget the long-term planning until you know there's going to be a long term. This makes perfect sense whether you are the zebra or the lion.

Now that you've put all of this glucose into your blood stream, you need to deliver it as fast as you can to your cells. Your heart rate will increase, your breathing quickens and your blood pressure rises. This gets the added energy to your thigh muscles in two seconds instead of three and makes you more likely to survive.

When you are in a moment of stress, your body turns off all sorts of long term building projects. This makes perfect sense - if there's a tornado due this afternoon, you're not going to spend the day outside gardening. Don't worry about the long-term projects until you know that there is going to be a long term.

Your body shuts down digestion because it is a long-term source of energy. The kind of energy that you need at the moment comes very quickly from your fat cells. If you are trying to avoid being someone's lunch, then don't worry about digesting your breakfast. In stress, our digestive tract shuts down. When we get nervous, our mouths gets dry - we stop secreting saliva. This is the first step towards shutting down the entire system.

During stress, we also shut down growth and reproduction. These are big, expensive, and optimistic projects for the body. If you're running from the lion, then we can afford to put off growing antlers or ovulating or reaching puberty. We shut down growth, tissue repair, and every sex hormone we have.



Also during stress, we shut down the immune system. Immunity is very important in fighting diseases, but it does not contribute very much to getting away from the lion over the next few minutes. Creating antibodies is an expensive project for the body, and once again, the body shuts down this process until a time when it knows that there will be a long

term.

Finally, the body secretes hormones that go into the brain and make us think very clearly in the short term. We feel more alert, our sensory thresholds are sharper, and our memory consolidation and retrieval gets faster. When your car spins out of control for three seconds, you will remember it as if it took three hours - we remember the details and nuances very clearly. I guarantee that all of us will remember exactly where we were and what we were doing when we heard that they were taking away Classic Coke, for example. We remember the big events in our lives, and it is the stress hormones that give us that clarity and strong awareness.

These are the things that we want our bodies to do if we are in a crisis like the lion or the zebra - mobilizing energy, delivering it to where it is needed, turning off the non-essentials and thinking more clearly. Most people can handle all of these functions pretty well. The people whose bodies cannot handle these functions tend to have pretty rare health conditions. They are not at risk for cancer or diabetes or heart disease, but if their bodies cannot handle any one of these functions, then they might just die suddenly while running across a parking lot.

Chronic Stress and Disease

Most of us do not have a problem in appropriately turning on the stress response. Most of us have a much bigger problem in appropriately turning it off. We turn on our stress response too often for too long and for purely psychological reasons. If you turn on your stress response chronically, you're going to get sick.

Selier was the first person to struggle with this dynamic of the stress-response. Short term stress response will save your life, but long term it will make you sick. Selier developed a theory that is now generally accepted as totally incorrect. Selier believed that if you remained stressed for too long, you would reach the "exhaustion phase" in which you would run out of your stress response. He believed that your adrenal gland and pituitary glands would run out of their hormones, and you would be left defenseless as the stressor hammers you. This never happens. No one on earth has ever run out of adrenaline. Our bodies never run out of "ammunition".

The real problem is that we spend so much on the defense budget that we cannot pay for health care, education, etc. (This is not a hidden social agenda, by the way.) In this way, the stress response becomes more damaging than the stressor ever was, especially if the stressor was some psychological nonsense that we invented in our own minds.

Eventually, the stress response is damaging because we shut down all of these long-term maintenance systems in our bodies to allow us to survive a short-term crisis. But if we invent psychological crises every day, then we never take the time to fix, repair, plan and grow.

At the metabolic level, if we are constantly mobilizing energy, we never take the time to store it. One of the main storage sites for energy in our bodies is the muscles. Muscles atrophy in people under stress because

they have tapped so deeply into the energy stores in their muscles. You also become at greater risk for adult-onset diabetes. This is yet another disease that our hunter-gatherer ancestors never heard of, yet it is the fifth leading cause of death in the US. Diseases associated with getting old can be caused by and worsened by stress.

At the cardiovascular level, if a lion is chasing us and our blood pressure is 180/120, we are saving our lives, not suffering from high blood pressure. If our blood pressure is 180/120 every time we have a conversation, however, we are not saving our lives. We are suffering from stress-induced hypertension. If you do that on a regular basis, you are going to get cardio-vascular disease.

Here is the typical story about stress and heart disease. A guy gets some stressful news, and suddenly clutches at his chest and keels over in sudden cardiac death. This never happens, except in the movies. The reasons that stress erodes your cardiovascular system are similar to the reasons that your house plumbing system wears out after awhile. This is basic fluid dynamics. Blood is moving through blood vessels, just like water is moving through pipes in your house. As the fluid moves through the vessels with greater force, the turbulence increases, and the fluid pounds harder on the walls of the vessels. Eventually you start to wear out the system. Your vessels develop scarring and plaques, and you set yourself up for cardiovascular disease - the number one killer of Americans.

Type A Personality and Toxic Hostility

The link between stress and heart disease is so solid that it is the cornerstone of the granddaddy of all stress-related psychological disorders - Type A Personality. Type A was originally defined in the 1950's by Freidman and Rosenman, a pair of cardiologists in San Francisco. Type A people are know by some common characteristics: time-pressured, hostile, impatient, low self-esteem, and joyless striving to check things off of the to-do list. Type A personality greatly increases your risk of heart disease. Cardiologists hated this. They were comfortable focusing on lipids and heart valves, but this diagnosis forced them to deal with the personalities of their patients, which is much messier. There was so much resistance among cardiologists to this approach that it took until the 1980's to finally gain widespread acceptance of the link between Type A and heart disease. Type A personality is the greatest risk factor for heart disease. It is a greater risk factor than if you smoke, if you are overweight, or elevated cholesterol levels.

The key factor of Type A personality is the "toxic hostility". These people interpret everything in the world around them as a personal attack or evidence that the world is out to get you. If you pick the wrong line in the supermarket, you will want to throttle that kid behind the cash register for being slow and making you late for your meeting. Type A's interpret everything as personal and globalized. If this is your response to every car that cuts you off in traffic, or every elevator door that closes when someone could have held it, you are going to raise your blood pressure. If you do this over a lifetime, you are going to get cardiovascular disease.

The current debate in this field is how Type A personalities should deal with their toxic hostility. Is it worse for your heart to express the hostility or to repress it? What is absolutely clear at this point is that expressing the hostility increases the stress of everyone around you. The debate is ongoing, however, about the impact of repression on the cardiovascular system.

One of the best demonstrations about how science is not supposed to work is the story of the original identification of the Type A personality. Meyer Freidman was the cardiologist who first described Type A personality in the 1950's. He and his partner's cardiology practice was going quite well in the 1950's, except for one problem - they were spending a fortune to reupholster the chairs in their waiting room. They didn't put too much thought into it, and figured that this was just part of the cost of doing business. Each month the upholsterer would come and redo a couple of the chairs. One month the regular upholsterer was on vacation, so a new guy came in, took one look at the chairs, and discovered Type A personality. "What the hell is wrong with your patients?" he asked. "Nobody wears out chairs like this!" The front two inches of the seat cushion and of the armrest had been shredded by Type A patients who had been squirming in their seats and clawing at the armrests.

Now if science worked the way that it is supposed to, then Freidman would have grabbed the upholsterer at this point and cried, "Good God, man! You have made a great discovery!" What actually happened, however, was that Freidman dismissed the upholsterer's comment out of hand. Freidman was too Type A to listen to him! Five years later, Friedman was working with a team of psychologists and out popped the Type A personality profile. Freidman thought to himself, "The upholsterer was right!" And yet to this day, they have no idea who the upholsterer was.

Impact on the Digestive Tract

What other kinds of stress-related problems can emerge? If you are chronically stressed, then you chronically shut down your digestive tract, then you are a good candidate for the most famous stress-related disorder - stomach ulcers. About ten years ago, there was a bit of a revolution in the ulcer world when they discovered a bacteria associated with ulcers. The gastrointestinal world went out and celebrated because if this was a disease caused by bacteria, then no doctors would ever have to sit down and talk with their patients about life and stress again.

Naturally, of course, stress is still the primary cause of ulcers, because only 10% of the people with the bacteria get ulcers. Many people have the same bacterial load, but they must be associated with a stressful risk-factor in order for ulcers to appear. This is the classic interaction between organic bases for disease and psychogenic bases of disease.

Impact on Growth

Kids are long-term building projects. If kids are under stress, then they shut down their growth. Taken to an extreme, you will find one of the truly bizarre outposts of medicine called Stress Dwarfism or Psychogenic

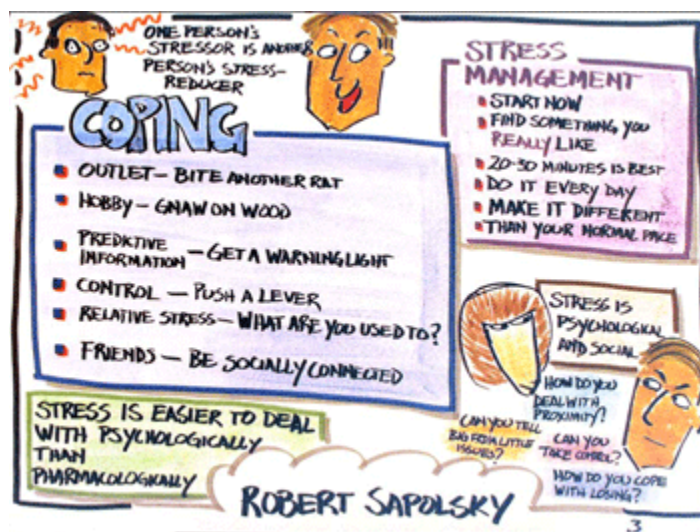
Dwarfism - where severe and prolonged stress induces kids to stop growing altogether. These kids are years behind the normal growth rates, and there are no diseases present and no parasites. There is no growth hormone in the blood stream, and even if you inject a synthetic growth hormone, it will not work. The amazing thing, however, is that if you remove the child from the stressful situation (do a "parent-ectomy"), they will tend to start growing again and catch up with the normal growth curves.

There was an incredible case study several years ago. A kid entered a hospital in New York from an extremely stressful and abusive home with zero growth hormone in his blood stream. Over first two months, he developed a very close relationship with one of the nurses - this was the first normal adult relationship that he had had in his life. At the end of two month, he had regained normal growth hormone levels in his blood. At this point, the nurse happened to go on vacation. By the end of her two-week vacation, the child had dropped back to no growth hormones in his blood stream. Three days after the nurse's return to work, his growth hormone was once again back to normal. The rate at which this child was depositing calcium in his long bones can be directly attributed to how safe and loved he was feeling. This is a demonstration that what happens in our minds affects every cell in the body.

The next question is how common this is. Stress Dwarfism is extremely rare. It cannot be caused by stresses like divorce or frequent relocations. These cases appear when the police and social workers break down the door to find a kid who's been locked in the closet - extreme psychopathology. The amazing part of this, though, is that if you remove the child from that setting, he will start to grow again.

When we look at kids in war zones and areas of civil strife, however, we discover that this rare disease is not so rare after all. My research assistant and I believe that we have enough data to demonstrate that kids in the Japanese internment camps during WWII had mild Stress Dwarfism. In the 1960's a pair of anthropologists studied the stress impacts of different rites of passage in cultures around the world. In one culture you might be taken out to the desert, staked down and covered with poison ant. In another culture you might have to play the piano for your grandmother. They studied 80 different cultures and discovered that in cultures with extremely stressful rites of passage, the average adult height was two inches shorter.

Now, let me tell you about the creepiest example of Stress Dwarfism that I have encountered. Many of the books that talk about growth hormones make references to Peter Pan. I could never figure out the connection until I ran across a particular case history. In the 1850's there was an eight year old boy growing up in Victorian England. One day he sees his beloved twelve year old brother killed in front of him in a horrible accident. This accident destroyed the family. There were no other siblings, and the older boy was the mother's favorite child. The father was absent. In typical Victorian fashion, the mother takes to her bed for the next ten years with the shades drawn. The young boy finds himself in total emotional isolation, having to deal by himself with all of these traumas.



He would walk into his mother's room with a tray of food, and his mother would ask, "David? David, is that you?" David was the dead son. When she realized it was the younger boy, she would say, "Oh, it's only you." Apparently the only thing that the mother would ever talk to the boy about was that if David had to die, at least he died when he was still young and perfect. He hadn't grown up to be one of those boys who no longer needed his mother. This way David would always remain that perfect little boy.

The younger brother heard all of this with a vengeance. This was a wealthy family, and the boy had no disease and no malnutrition, yet the boy stopped growing. He lived to be 60 years old and 4'10". It was confirmed in his autopsy that he never reached puberty. This is a perfect example of Stress Dwarfism.

This case history ends with an interesting twist. As an adult, this person was the author of the much-beloved children's book, Peter Pan. This was JM Barry. In 1910, this was the most widely-read author in the US. His entire career focused on writing books and plays and novellas about boys and death and oedipal situations. He was repeatedly in trouble for sadomasochistic relationships with young boys. He spent half of his fortune keeping these stories out of the newspapers. He spent his entire life unsuccessfully dealing with his Stress Dwarfism.

Impact on Female Sex Hormones

Now, we are fine if we shut down our sexual hormones for a few minutes to get away from the lion, but if we shut them down chronically, the system will have trouble functioning. Female mammals under chronic stress have very irregular menstrual cycles. We understand how this works extremely well, but there is an interesting twist. Females excrete a

certain amount of male sex hormones from their adrenal glands. These are called adrenal androgens. They do not excrete much of this hormone, but they need to get it out of their systems. Fortunately in mammals, there is an enzyme in the fat cells that can convert the androgens into estrogen. If you are suffering from stress associated with malnutrition, however, then you deplete your fat cells to the point where there are not enough of them to convert all of the androgen to estrogen. Androgen levels build up, and that shuts down the female reproductive system. This is why starvation shuts down ovulation. This is also why voluntary starvation - anorexia - does the same. One of the hallmarks of anorexia is that ovulation stops very early in the process.

This is the reason that women who do a lot of athletics stop ovulating. They get below the critical threshold of fat stores in their bodies. This brings up a very important point that shows up repeatedly in our studies. Girls who do a lot of athletics (ballet or gymnastics, for example) experience a major delay in the onset of puberty. A few years ago, the average age for the onset of menstruation for the Olympic gymnastics squad from Romania was nineteen years old. Twelve and a half is the average age in the western world. The level of exercise that gets you into trouble is running 40-45 miles per week. Males suffer the same effects. Running 40-45 miles per week tends to suppress testosterone levels and lead to testicular atrophy.

Now, isn't exercise supposed to be good for you? Exercise is good for you, and a lot of exercise is very good for you, but that does not mean that an insane amount of exercise is insanely good for you! Too much of a good thing is just as bad as too little. Either way, you are knocking yourself out of homeostatic balance. Imagine the reaction of a hunter-gatherer if you told him that we have so much food and so much free time that sometimes we go out and run 26 miles in a day for the sheer pleasure of it. He would think that you are crazy! That much running is stressful! If he had to run 26 miles in a day, then either he is really intent on eating something or something is very intent on eating him. This is not normal hominid behavior.

Impact on Male Sex Hormones

On the male side of the equation, stress tends to reduce testosterone levels. If you measure testosterone levels during surgery, you will see them drop as the body is under stress. Testosterone drops for first-year male medical students during exam time. If you manipulate a male baboon's rank so that he drops on the hierarchy, and his testosterone levels will drop as well. Apparently the Marine Corps boot camp is so stressful that the androgen levels of men in their first few weeks of the Marines are about the level of Vatican choir boys. The system is deeply suppressed by this stress, and we fully understand the mechanics of how this happens.

What are the consequences of decreased androgen levels? Interestingly enough, there are no consequences whatsoever! It turns out that testosterone is a vastly overrated hormone. Men need about a thimbleful of testosterone to function properly. You would need to knock out about 90% of a man's testosterone levels to impair the system. Stress only ever suppresses the system by 60-70%.

The trouble for men during stress is not that the testosterone goes down but that the penises go down. Let me tell you about erections. Most of your spinal chord is responsible for boring things like shaking hands and signing checks, but there is a part of the spinal chord that does the good stuff that you normally have no control over - goose flesh, orgasms, shivers, pupillary contractions, and anything else that's automatic. This is the autonomic nervous system, and it comes in two halves. The sympathetic nervous system deals with fear, arousal and emergency situations. The parasympathetic nervous system deals with the vegetative, relaxed state. If you take a nap, you turn on the parasympathetic system. If you get mauled by a lion, you turn off the parasympathetic and turn on the sympathetic. These two systems work in opposition.

In order to have an erection, you have to turn on the parasympathetic nervous system - you have to be calm and vegetative. Once you have the erection, then something about the social context which brought about the erection in the first place might make you feel a little less calm and vegetative. You might start breathing a little faster. Maybe your heart starts beating a little faster. You are slowly turning on the sympathetic nervous system. As more time goes by and you are breathing hard and sweating and curling your toes, and your entire body is screamingly sympathetic, there is still one lone outpost that's desperately holding on the parasympathetic for as long as possible. Finally when you cannot hold on any longer, you turn off the parasympathetic, turn on the sympathetic and ejaculate. So, that's how erections work.

The challenge during stress is that you are not very calm and vegetative, and you therefore cannot get an erection. This is stress-induced impotency. The second problem that could occur is premature ejaculation - stress accelerates the transition from parasympathetic to sympathetic. 60% of the cases of erectile dysfunction in the US are caused by psychology, not organic problems. It is stress-related.

How can you tell the difference between organic impotency and psychogenic impotency? How can you tell if someone is suffering from stress-related impotency or a spinal problem or tumor? You can take advantage of a very strange quirk of male primates - when they go into REM (Rapid Eye Movement) sleep, they get erections. I have talked to the earth's penis experts, and no one understands why this happens, but it does.

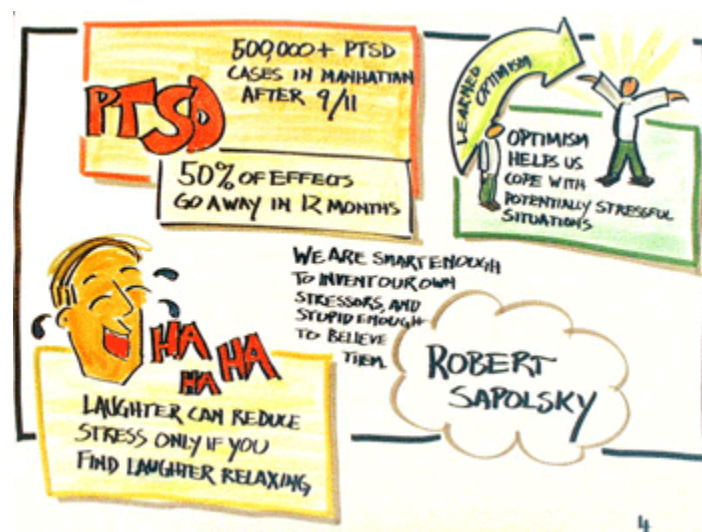
So, to determine if a man's erectile dysfunction is stress-induced or physical, you can give him a handy dandy penile pressure cuff transducer thingie that he takes home and puts on before he goes to bed. This device gets wired into a satellite relay, and the next morning the computer tells you whether or not the man has had an erection during REM sleep. Even if a man has not been able to have an sexual erection for six months, if he can have a nocturnal erection, then his dysfunction is stress-related, not organic in nature.

This sounds easy enough, but the device is actually quite expensive and complicated. There are wires all over the place, and it feels as though

you might electrocute yourself, which is a stressor in and of itself! I recently discovered a much better way of doing this test. Take a string of postage stamps, lick them, and wrap them around the base of the penis before going to bed. (I will not specify how many stamps should be required.) In the morning, if the stamps have been torn loose at one end, then there was a nocturnal erection! What an elegant solution! For three dollars, you get a lab result. Of course, insurance won't pay for it...

Impact on the Immune System

Shutting down your immune system for three minutes is fine, but shutting it down chronically can cause you some real problems. This is a whole new field of study - psycho-neuro-immunology. The theory is that if chronic stress chronically reduces immunity, then people who suffer from chronic stress will suffer from more infectious diseases. This field is about ten years old, and has shown that this is indeed the way it works for the boring stuff - the common cold, mononucleosis, herpes cold sore flare-ups, etc.



The debate is still ongoing around the big diseases. If you have HIV, will stress accelerate the decline of your immune system? The jury is still out. We are all most worried about the relationship between stress and cancer. It is common knowledge the stress can cause cancer and that it can accelerate an existing cancer. This is a widely-held belief, and studies of breast-cancer patients have shown most people believe their cancer to be caused by stress.

There is no scientific evidence that stress can cause cancer, and there is only a tiny bit of evidence that stress can accelerate a pre-existing cancer. Stress has nothing to do with cancer. This is an important lesson to share because there are all sorts of quacks out there selling products by convincing people that cancer is stress-related. This is bad science

and bad clinical medicine. This is one area in which stress is not relevant.

Impact on the Brain

Finally, the same hormone that make you think so clearly during stress will eventually kill your brain cells if they are activated chronically. They kill a class of neurons that handle learning and memory. My lab has spent the last 20 years studying this area - whether stress increases the likelihood of Alzheimer's, for example, because these hormones affect the same part of the brain. Do these hormones determine why some people age more gracefully than others in terms of cognitive intactness? Until a few years ago this was pure speculation, but we have learned that this is highly related to humans. In the last few years, we have identified two disorders that come about because of atrophy in the brain due to stress - Post Traumatic Stress Disorder and Chronic Depression.

If you are not already depressed, let me tell you about one more stress-related disorder. Idiopathic Alopecia Areata is a profoundly rare state in which you are so deeply stressed and traumatized that over the next couple of days, your hair turns white and falls out. This is a real disease, even though a dermatologist might see one case in a whole career.

Coping with Stressors

So stress gives us high blood pressure, reproductive problems, heart disease, flatulence, sexual problems, and makes our hair fall out. How is it that any of us are still alive? Because most of us have not collapsed into a puddle of stress-related disease, it is clear that we have developed mechanisms to cope. Some bodies and some psyches are better at coping with stress than others. There are several factors that contribute to our varying abilities to cope with stress.

At this point, I am not talking about physical stressors. Go outside of this room and unexpectedly be gored by an elephant, and you're going to have a stress-response. You cannot prevent such a response from a physical stimulus. If you go outside of this room and have an ambivalent conversation with a friend, and you might or might not have a stress-response. The critical point is that what is a tremendous stressor for one person will be someone else's favorite hobby. There are tremendous individual differences in degrees of stress associated with the large grey area of social interactions. What makes stress stressful? What makes a particular situation stressful for one person and not stressful for someone else?

There has been a tremendous amount of work done to identify the building blocks of psychological stress. The kinds of experiments that are done start by putting a rat in a cage with an electrified floor so that you can give the rat a mild shock. Each shock is not especially painful, but with enough shocks, the rat gets stressed. Its hormone levels, its heart rate and its risk of an ulcer all go up. We are giving the rat a stress-related disease.

1. Outlet for Frustration

In the next cage, there is a second rat. It is "yoked" to the first rat, so that each time the first rat receives a shock, so does the second rat, with the

same duration and intensity. Both of these rats are being knocked equally out of homeostatic balance, and therefore the impacts on their bodies should be the same. The second rat, however, has some support. Every time he gets shocked, he can go over into a corner and bite yet another rat. The second rat never develops an ulcer! (The rat getting bitten certainly does, of course.) The second rat does not develop an ulcer because he has an outlet for his frustration.

2. A Hobby

In the next experiment, the second rat gets the same shock at the first, except he can gnaw on a bar of wood that is in his cage. Again, the second rat never develops an ulcer - it has a hobby!

3. Predictive Information

In the third experiment, the second rat gets the same shock as the first rat, but ten seconds before each shock, a warning light comes on. The rat does not develop an ulcer. For the same physical stressor, you are less likely to get a stress related disease if you get predictive information - when is it coming, how bad is it going to be? This is the same principle that we all use in the dentist chair when we ask, "Are we almost done?" We just want predictive information. A good dentist will tell you that you've got two more bits of drilling to do. The bad news is that the procedure is not yet over, but as soon as that second bit of drilling is done, you know that you can relax. The rat without the warning light is always stressed because he does not know when the next shock is coming. He never knows when he is safe.

4. Sense of Control

In the fourth version of the experiment, the second rate has been trained to press a lever. In the training, when it pressed the lever, it was less likely to receive a shock. In the live experiment, the lever is disconnected - it has no effect on whether or not the rat gets the shock. Nevertheless, the rat will pound away on the lever, get the same shocks as the first rat, and yet never develop an ulcer. It thinks it has control. A sense of control (whether or not it is real) makes stressors less stressful.

5. Interpretation

In the next experiment, the first rat is used to receiving ten shocks per hour while the second rat is accustomed to receiving fifty shocks per hour. In the experiment, both rats receive twenty-five shocks per day. The rat that is used to only ten shocks develops an ulcer, while the second rat does not. Our stress level is based on our perception and our interpretation. The level of stress associated with a particular situation depends entirely on what you are used to.

About thirty years ago there was a study done of parents whose children had a 25% chance of dying of cancer. Their stress levels should have been through the roof, and yet they were remarkably low. The reason they were so low was that their cancers were in remission - a short time earlier, they had been parents of kids with a 90% chance of dying of cancer. If you were the parent of a perfectly health child who suddenly developed a 25% chance of dying, it would be horrible. But if your child had started with a 90% probability of death, then a 25% probability would feel like a blessing. The situation means entirely different things

depending on which direction you came from.

6. Social Connectedness

In the final experiment, put the second rat in a cage with another rat that it knows and likes. The rat does not get an ulcer. Science has finally proven to us that friends are good for your health. Across all disease types, the greatest predictor of mortality is socioeconomic status. Your health is going to be worse if you are poor. After you control for socioeconomic status, however, the next biggest predictor of mortality is your degree of social connectedness. There is almost a three-fold difference in survival rate between the most isolated person and the most socially affiliated person. This is also after you control for all of the factors associated with living alone - like no one to give them medicine, and eating only Cheetos for dinner. Being socially isolated is a major stressor and a health risk factor for every primate including humans.

Conclusions

For the same external stressor, you are more likely to get a stress related disease if you feel that you do not have outlets, if you do not have predictive information about the stressor, if you have no sense of control, if you interpret things as getting worse, and if you have nobody's shoulder to cry on. None of us is going to get ulcers because the locusts have eaten our crops or because we have had to fight for canned food items. Most of us are sufficiently ecologically buffered enough that we have the luxury of making up this stuff in our heads.

Insofar as we are a species that is cognitively sophisticated enough to invent with this stuff, and then we are stupid enough to fall for it, all of us have the potential to be wise enough to keep this in perspective.

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