

Stress - InDepth

Highlights

Overview

- Nearly everyone experiences stress at some time. Stress produces changes in the body such as increased heart rate, blood pressure, and altered immune function.
- Some amount of stress is healthy, but excessive chronic stress, left untreated, can increase a person's risk for anxiety and illness.

Causes

- Major causes of chronic psychological stress include work, money, family responsibilities, and health concerns. Unhealthy habits such as overeating or eating unhealthy foods can result from stress.

Risks

- The combined effect of job stress and an unhealthy lifestyle poses the highest risk for coronary heart disease (CHD) compared to either factor alone. Among those with job strain, making healthy lifestyle choices can lower the risk of developing CHD significantly.
- In pregnant women, chronic stress can lead to problems with the baby, such as low birth weight. Screening and intervention strategies may help to improve outcomes.
- In people with atherosclerosis, acute or chronic mental stress can induce heart disease and increase the risk for a heart attack. Researchers are looking at the effectiveness of medications, such as escitalopram, in reducing the risk of mental stress-induced myocardial ischemia (MSIMI).

Stress Reduction Therapy

- Several strategies have been shown to help reduce stress, such as exercise, practicing mindfulness-based stress reduction (meditation and yoga), acceptance and commitment therapy (ACT), and participating in a cognitive behavioral therapy (CBT) program.
- CBT has been shown to help reduce the stress associated with many chronic medical conditions, including back pain, arthritis, and tinnitus (buzzing in the ears).
- Meditation may help ease symptoms of anxiety, depression, and pain, but its role in modulating positive mood, attention, substance use, eating habits, sleep, and weight gain is less clear.
- Certain medications may help to treat specific post-traumatic stress disorder (PTSD) symptoms, such as trauma nightmares.
- Several pilot projects are underway to assess the effects of "virtual healing" using devices such as video game simulators that might augment traditional stress management therapies.
- Internet-based approaches are improving access to guided self-help psychological interventions.

Introduction

Stress affects most people in some way. Acute (sudden or short-term) stress leads to rapid changes throughout the body. Almost all body systems (the heart and blood vessels, immune system, lungs, digestive system, sensory organs, and brain) gear up to meet perceived danger.

These stress responses could prove beneficial in a critical, life-or-death situation. Over time, however, repeated stressful situations put a strain on the body that may contribute to physical and psychological problems. Chronic (long-term) stress can have real health consequences and should be addressed like any other health concern.

Fortunately, research is showing that lifestyle changes and stress-reduction techniques can help people manage stress.

External and Internal Stressors

People can experience stress from external or internal factors.

- External stressors include adverse physical stimuli (such as pain or hot or cold temperatures) or stressful psychological environments (such as poor working conditions or abusive relationships).
- Internal stressors can also be physical (infections and other illnesses, inflammation) or psychological (such as intense worry about an event that may or may not occur).

Acute or Chronic Stress

Stressors can also be defined as short-term (acute) or long-term (chronic).

Acute Stress

Acute stress is the reaction to an immediate threat, commonly known as the **fight or flight** response, and is accompanied by the release of stress hormones. The threat can be any situation that is perceived, even subconsciously or falsely, as a danger.

Common acute stressors include:

- Noise (which can trigger a stress response even during sleep)
- Crowding
- Isolation
- Hunger
- Danger (such as while driving)
- Infection
- High technology effects (such as playing video games or frequently ringing mobile phones)
- Imagining a threat or remembering a dangerous or traumatic event

Under most circumstances, once the acute threat has passed, levels of stress hormones return to normal. This is called the **relaxation response**.

Chronic Stress

Frequently, modern life exposes people to long-term stressful situations. Stress, then, becomes persistent and chronic. The urge to act (to fight or flee) must therefore be controlled.

Common chronic stressors include:

- Ongoing work pressure
- Long-term relationship problems
- Loneliness
- Persistent financial or health worries

The Body's Response

The best way to envision the effect of acute stress is to imagine yourself in a primitive situation, such as being chased by a bear.

The Brain's Response to Acute Stress

In response to seeing the bear, a part of the brain called the **hypothalamic-pituitary-adrenal (HPA)** system is activated.

Release of Steroid Hormones and the Stress Hormone Cortisol

The HPA system triggers the production and release of steroid hormones (**glucocorticoids**), including the primary stress hormone **cortisol**. Cortisol is very important in organizing systems throughout the body (including the heart, lungs, circulation, metabolism, immune systems, and skin) to deal quickly with the bear.

Release of Catecholamines

The HPA system also releases certain neurotransmitters (chemical messengers) called *catecholamines*, particularly those known as **dopamine**, **norepinephrine**, and **epinephrine** (also called adrenaline).

Catecholamines activate an area inside the brain called the **amygdala**, which appears to trigger an emotional response to a stressful event. In the case of the bear, this emotion is most likely fear.

Release of Neuropeptide S

The brain releases neuropeptide S, a small protein that modulates stress by decreasing sleep and increasing alertness and a sense of anxiety. This gives the person a sense of urgency to run away from the bear.

Effects on Long- and Short-Term Memory

During the stressful event, catecholamines also suppress activity in areas at the front of the brain concerned with short-term memory, concentration, inhibition, and rational thought. This sequence of mental events allows a person to react quickly, either to fight the bear or to flee from it. It also interferes with the ability to handle difficult social or intellectual tasks and behaviors during that time.

At the same time, neurotransmitters signal the **hippocampus** (a nearby area in the brain) to store the emotionally loaded experience in long-term memory. In primitive times, this brain action would have been essential for survival, because long-lasting memories of dangerous stimuli (such as the large bear) would be critical for avoiding and dealing with such threats in the future.

Research also finds that during times of stress, nerve cells in the brain interpret chemical signals incorrectly. Instead of switching "off," these nerve cells perceive the signals as telling them to switch "on." It is as though the brain's "brakes" fail in response to stress.

Response by the Heart, Lungs, and Circulation to Acute Stress

The stress response also affects the heart, lungs, and circulation:

- As the bear comes closer, the heart rate and blood pressure increase instantaneously.
- Breathing becomes rapid, and the lungs take in more oxygen.
- The spleen discharges red and white blood cells, allowing the blood to transport more oxygen throughout the body.
- The cardiac output may actually increase 300% to 400%, priming the muscles, lungs, and brain for added demands.

The Immune System's Response to Acute Stress

The effect of confronting the bear on the immune system is similar to mobilizing a defensive line of soldiers to potentially critical areas. The steroid hormones reduce activity in parts of the immune system, so that specific infection fighters (including important white blood cells) or other immune molecules can be repositioned. These immune-boosting troops are sent to the body's front lines where injury or infection is most likely to occur, such as the skin and the lymph nodes.

The Acute Response in the Mouth and Throat

As the bear gets closer, blood flow decreases to nonessential locations, including the digestive system. This causes dry mouth and difficulty talking. In addition, stress can cause spasms of the throat muscles, making it difficult to swallow.

The Skin's Response to Acute Stress

The stress effect moves blood flow away from the skin to support the heart and muscle tissues. This also reduces blood loss in the event that the bear causes a wound. The physical effect is cool, clammy, sweaty skin. Tiny muscles attached to hair follicles contract to cause what is known as "goose bumps". The scalp also tightens so that the hair seems to stand up.

Other Responses to Acute Stress

Stress relaxes intestinal muscles and reduces digestive activity, a body function that is not essential during short-term periods of hard physical work or crisis. Bladder muscles relax, so that urination is also inhibited. Pupils dilate to allow more light to hit the retina. More glucose is released in the blood to provide a quick energy boost for the brain and muscles.

The Relaxation Response

The Resolution of Acute Stress

Once the threat has passed without any harmful outcome (for example, the bear has not wounded the human), the stress hormones return to normal. This is known as the **relaxation response**. In turn, the body's systems also return to normal.

Risk Factors for Stress

At some point in their lives, virtually everyone will experience stressful events or situations that overwhelm their natural coping mechanisms. Some people are simply biologically prone to stress. Many outside factors influence susceptibility as well.

Conditions Most Likely To Produce Stress-Related Health Problems

Conditions that are most likely to be associated with stress and negative physical effects include the following:

- An accumulation of persistent stressful situations, particularly those that a person cannot easily control (for example, a high-pressure job plus an unhappy relationship)
- Persistent stress after a severe acute response to a traumatic event (such as an automobile accident)
- Acute stress accompanying a serious illness, such as heart disease

Factors That Influence the Response to Stress

People respond to stress differently, depending on different factors:

- **Early nurturing.** People who were abused or stressed in childhood may have long-term abnormalities in the HPA system, which regulates stress.
- **Personality traits.** Certain people have personality traits that cause them to over-respond to stressful events. For example, those who are neurotic may get stressed more easily and turn to unhealthy behaviors such as smoking and heavy drinking as a result. Being more outgoing and aware of the world may improve a person's response to stress by lowering levels of stress-related inflammatory hormones.

- **Genetic factors.** Some people have genetic factors that affect stress, such as having a more or less efficient relaxation response.
- **Immune regulated diseases.** Certain diseases that are associated with immune abnormalities (such as rheumatoid arthritis or eczema) may weaken the response to stress.
- **The length and quality of stressors.** The longer the duration and the more intense the stressors, the more harmful the effects.

Individuals at Higher Risk for Stress

Studies indicate that the following people are more vulnerable than others to the effects of stress:

- **Older adults.** As people age, achieving a relaxation response after a stressful event becomes more difficult. Aging may simply wear out the systems in the brain that respond to stress, so that they become inefficient. Older people too are very often exposed to major stressors such as medical problems, the loss of a spouse and friends, a change in a living situation, and financial worries. No one is immune to stress, however.
- **Women in general and working mothers specifically.** Working mothers, regardless of whether they are married or single, face higher stress levels and possibly adverse health effects, most likely because they bear a greater and more diffuse workload than men or other women. This effect has been observed in women in the United States and in Europe. Such stress may also have a harmful effect on their children.
- **Less educated individuals.** Studies show that people with lower educational qualifications experience more work-related stress.
- **Divorced or widowed individuals.** Numerous studies indicate that unmarried people generally do not live as long as their married contemporaries.
- **Anyone experiencing financial strain.** Particularly the long-term unemployed and those without health insurance.
- **People who are isolated or lonely.**
- **People who are targets of racial, sexual, or other types of discrimination.**
- **People who live in cities.**

Childhood Factors

Children are frequent victims of stress because they are often unable to communicate their feelings accurately. They also have trouble communicating their responses to events over which they have no control. Certain physical symptoms, notably repeated abdominal pain without a known cause, may be indicators of stress in children.

Various conditions can affect a child's susceptibility to stress.

Parental Stress

Parental stress, especially in mothers, is a particularly powerful source of stress in children. Young children of mothers who are highly stressed (particularly if they are also depressed) tend to be at high risk of developing stress-related problems. This may be especially true if the mothers were stressed during both the child's infancy and early years. Stressed parents may even make their children more likely to develop asthma. Some evidence supports the old idea that stress during pregnancy can have adverse effects on the infant's mood and behavior. Older children with stressed mothers may become aggressive and anti-social. Stress-reduction techniques in parents may improve their children's behavior.

Gender Differences in Adolescent Stress

Adolescent boys and girls experience equal amounts of stress, but the source and effects may differ. Girls tend to become stressed from interpersonal situations, and stress is more likely to lead to

depression in girls than in boys. For boys, however, specific events, such as changing schools or getting poor grades, appear to be the major sources of stress.

Work and Stress

Health care costs are much higher in workers who are stressed or depressed than in others who are not stressed. Nearly one-half of American workers describe their jobs as very stressful, making job-related stress an important and preventable health hazard. In a struggling economy, worry about job loss produces a tremendous amount of stress.

Several studies are now suggesting that job-related stress is as great a threat to health as smoking or not exercising. Stress impairs concentration, causes sleeplessness, and increases the risk for illness, back problems, accidents, and lost time from work. Work stress can lead to harassment or even violence on the job. At its most extreme, chronic stress places a burden on the heart and circulation that in some cases may be fatal.

Not all work stress is harmful. However, studies suggest the following job-related stressors may increase health risks, particularly in men:

- Having no control over decisions that affect one's responsibilities
- Unrelenting and unreasonable performance demands
- Lack of effective communication and conflict-resolution methods among workers and employers
- Lack of job security
- Night-shift work, long hours, or both
- Spending too much time away from home and family
- Wages not matching levels of responsibility

Reducing Stress on the Job

Many companies put intense pressure on their employees to behave in ways that increase tension. Yet, there are numerous effective tools and techniques available to reduce stress, and have proven beneficial for both the employee and employer. Studies show that stress management programs save in workers compensation costs, and may lower employees' blood pressure.

In general, however, few workplaces offer stress management programs, and it is usually up to the employees to find their own ways to reduce stress. Here are some suggestions:

- Seek out someone in the Human Resources department or a sympathetic manager and communicate concerns about job stress. Work with them in a non-confrontational way to improve working conditions, letting them know that productivity can be improved by reducing the pressure on employees.
- Establish or strengthen a network of friends at work and at home.
- Restructure priorities and eliminate unnecessary tasks.
- Learn to focus on positive outcomes.
- If the job is unendurable, plan and execute a career change. Send out resumes or work on getting a transfer within the company.
- If this is not possible, be sure to schedule pleasant activities and physical exercise every day during free time.

Caregiving

Caregivers of Family Members

Studies show that caregivers of physically or mentally disabled family members are at risk for chronic stress. Spouses who care for a disabled partner are particularly vulnerable to a range of stress-related

health threats, including influenza, depression, and heart disease. Caring for a spouse who has even minor disabilities can lead to severe stress.

Specific risk factors that put caregivers at higher risk for severe stress, or stress-related illnesses, include:

- Being a woman. Some studies suggest that wives experience significantly greater stress from caregiving than men.
- Having a low income.
- Living alone with a patient.
- Helping a highly dependent person.
- Having a difficult relationship with a person.

Intervention programs aimed at caregivers can help reduce stress, and help the caregiver maintain a positive attitude. Moderate-intensity exercise can also be very helpful in reducing stress and improving sleep in caregivers.

Health Professional Caregivers

Caregiving among health professionals is also a high risk factor for stress. One study found that registered nurses with low job control, high job demands, and low work-related social support experienced very dramatic health declines, both physically and emotionally.

Anxiety Disorders

People who are less emotionally stable or who have high anxiety levels tend to experience specific events more stressfully than others. Some doctors describe an exaggerated negative response to stress as "catastrophizing" the event (thinking of a problem as a catastrophe). However, research has found that patients with anxiety disorder do not have any differences in their actual physical response to stress (such as heart rate, blood pressure, or release of stress hormones) compared to people without anxiety.

Lacking a Social Network

The lack of an established network of family and friends predisposes a person to stress disorders and stress-related health problems, including heart disease and infections. Older people who maintain active relationships with their adult children are buffered against the adverse health effects of chronic stress-inducing situations, such as low income or lower social class. This may be because people who live alone are unable to discuss negative feelings to relieve their stress.

People who remain happy and healthy despite many life stresses typically have very good social support networks. Having a pet may help reduce medical problems that are aggravated by stress, including heart disease and high blood pressure.

Complications

In prehistoric times, the physical changes in response to stress were an essential adaptation for meeting natural threats. Even in the modern world, the stress response can be an asset for raising levels of performance during critical events, such as a sports activity, an important meeting, or in situations where there is actual danger or a crisis.

When low-level stress becomes persistent, all parts of the body's stress apparatus (the brain, heart, lungs, blood vessels, and muscles) become chronically over-activated or under-activated. Such chronic stress may produce physical or psychological damage over time. Acute stress can also be harmful in certain situations, particularly in individuals with pre-existing heart conditions.

Psychological Effects of Stress

Studies suggest that the inability to adapt to stress is associated with the onset of depression or anxiety.

Some evidence suggests that the repeated release of stress hormones produces hyperactivity in the hypothalamic-pituitary-adrenal (HPA) system, and disrupts normal levels of serotonin, the brain chemical that is critical for feelings of well-being. Some people appear to be more at risk for an overactive HPA system under stress, including those with personality traits that tend towards perfectionism. On a more obvious level, stress reduces quality of life by affecting feelings of pleasure and accomplishment. In addition, relationships are often threatened in times of stress.

Heart Disease

The full impact of mental stress on heart disease is just coming to light, but the underlying mechanisms are not always clear. Stress can influence the activity of the heart when it activates the automatic nervous system. Such actions and others could negatively affect the heart in several ways:

- Sudden stress increases the pumping action and rate of the heart, while at the same time causing the arteries to constrict (narrow). As a result blood pressure rises.
- The emotional effects of stress alter the heart rhythms, which could pose a risk for serious arrhythmias (rhythm abnormalities) in people with existing heart rhythm disturbances.
- Stress causes certain blood cells to become stickier (possibly in preparation for potential injury) which makes blood clotting, especially in vulnerable arteries of the heart and brain, more likely.
- Stress appears to impair the clearance of fat molecules in the body.
- Stress that leads to depression appears to be associated with increased intima-medial thickness, a measure of the arteries that signifies worsening blood vessel disease.
- Stress causes the body to release inflammatory markers into the bloodstream. These markers may worsen heart disease or increase the risk of a heart attack or stroke.
- Studies have reported an association between stress and high blood pressure, which may be more pronounced in men than in women. According to some evidence, people who regularly experience sudden spikes in blood pressure (caused by mental stress) may, over time, develop injuries to the inner lining of their blood vessels.

Evidence is still needed to confirm any clear-cut relationship between stress and heart disease. However, research has linked stress to heart disease in men, particularly in work situations where they lack control. The association between stress and heart problems in women is weaker, and there is some evidence that the ways in which women cope with stress may be more heart-protective.

The combined effect of job stress and an unhealthy lifestyle poses a higher risk for coronary heart disease (CHD) than either factor alone. Among those with job strain, making healthy lifestyle choices can lower the risk of developing CHD significantly.

A condition called **stress cardiomyopathy** (or Takotsubo cardiomyopathy) is widely recognized. In this disease, intense emotional or physical stress causes severe but reversible heart dysfunction. The person experiences chest pain, and electrocardiograms (EKGs) and echocardiograms indicate a heart attack, but further tests show no underlying obstructive coronary artery disease.

For those already with heart disease, an increase in physical activity can stress the heart and cause ischemia (a drop in oxygen supply to the heart muscle). Mental stress appears to also have the same ability to cause ischemia and possible angina. Psychological stress is also recognized as a possible cause of acute coronary syndrome (ACS), a collection of symptoms that indicate a heart attack or approaching heart attack. Studies also suggest that the risk is greatest immediately after a stressful incident, rather than during it.

Researchers are looking at the effectiveness of medications, such as escitalopram, in reducing the risk of mental-stress induced myocardial ischemia (MSIMI), a condition characterized by reduced blood supply to the heart. More research is necessary, however.

Stress Reduction and Heart Disease

Studies suggest that treatments that reduce psychological distress improve the long-term outlook in people with heart disease, including after a heart attack. Evidence indicates that stress management programs may significantly reduce the risk for heart attacks in people with heart disease. Specific stress management techniques, such as relaxation techniques, may help some heart problems but not others.

Stroke

In some people, prolonged or frequent mental stress causes an increase in blood pressure, a risk factor for stroke and heart disease. Job strain may be associated with an increased risk for stroke.

Effect on the Immune System

Chronic stress affects the immune system in complicated ways and may have various results.

Susceptibility to Infections

Chronic stress may reduce the immune system's response to infections. Several studies claim that people who are under chronic stress have low white blood cell counts and are more vulnerable to colds. Once a person catches a cold or flu, stress can make symptoms worse. People who carry the herpes virus may be more susceptible to viral activation after they are exposed to stress.

Inflammatory Response

Some evidence suggests that chronic stress triggers an over-production of certain immune factors called cytokines. Such findings may partly explain the association between chronic stress and numerous diseases, including heart disease and asthma.

Cancer

A relationship between excess stress and cancer has not been proven. Evidence has shown that job stress is not a significant risk for colorectal, breast, prostate, or lung cancer. Although stress reduction techniques have no effect on survival rates, studies show that they are very helpful in improving a cancer patient's quality of life.

Gastrointestinal Problems

Prolonged stress can disrupt the digestive system, and increase the occurrence of diarrhea, constipation, cramping, bloating, and acid reflux.

Irritable Bowel Syndrome (IBS)

IBS (or spastic colon) is strongly related to stress. With this condition, the large intestine becomes irritated, and its muscular contractions are spastic rather than smooth and wave-like. The abdomen is bloated, and the patient experiences cramping and alternating periods of constipation and diarrhea. Sleep disturbances due to stress can make irritable bowel syndrome even worse.

Peptic Ulcers

It is now well established that most peptic ulcers are caused by *H pylori* bacteria or the use of nonsteroidal anti-inflammatory (NSAID) medications (such as aspirin and ibuprofen). Not all *H pylori*

carriers develop peptic ulcers, and studies still suggest that stress may predispose a person with *H pylori* to ulcers.

Additionally, emotional stress may increase the risk for health behaviors that are clearly associated with peptic ulcer disease, such as alcohol use and cigarette smoking.

Inflammatory Bowel Disease

Although stress is not a cause of inflammatory bowel disease (Crohn disease or ulcerative colitis), there are reports of an association between stress and symptom flare-ups.

Eating and Stress

Stress can have varying effects on eating problems and weight. Many Americans report overeating, eating unhealthy foods, or skipping meals due to stress. Both weight gain and weight loss can be related to appetite problems due to stress.

Weight Gain

Often stress is related to weight gain and obesity. Many people develop cravings for salt, fat, and sugar to counteract tension. As a result, they gain weight. In addition, the weight gained is often abdominal fat, which increases the risk of developing diabetes and heart problems. Family stress also appears to contribute to childhood obesity.

The release of cortisol, a major stress hormone, appears to boost abdominal fat and may be the primary connection between stress and weight gain. Cortisol is a glucocorticoid. These hormones, along with insulin, appear to be responsible for stress-related food cravings. Evidence suggests that hormonally induced cravings for "comfort foods" may have a biological benefit for managing stress. Eating comfort foods appears to reduce the negative hormonal and behavioral changes associated with stress, which might lessen the impact of stress on an individual. Carbohydrates in particular may increase levels of tryptophan and large neutral amino acids. This leads to more production of the chemical messenger serotonin, which might improve mood and performance under stress.

There may be a "reward-based stress eating" model. In this theory, both stress and tasty, high-calorie foods cause the brain to make chemicals called endogenous opioids. These neurotransmitters help protect against the harmful effects of stress, slowing activity of a brain process called the hypothalamic-pituitary-adrenal (HPA) axis, thus weakening the stress response. Repeated stimulation of the reward pathways through stress-induced HPA stimulation, eating tasty food, or both, may lead to changes in the brain that cause compulsive overeating.

Eating Disorders

Chronically elevated levels of stress chemicals have been observed in people with anorexia and bulimia. Some studies, however, have not found any strong link between stress and eating disorders. More research is needed to determine whether changes in stress hormones are a cause or a result of eating disorders.

Diabetes

Stress can exacerbate existing diabetes by impairing the patient's ability to manage the disease effectively. Stress-induced weight gain will further worsen the disease.

Pain

Researchers are attempting to find the relationship between pain and stress. The response to stress is complicated by many factors, including the effects of different personality types, and the fear of pain

and stress itself. Evidence suggests that chronic pain may impair the action of neutrophils, a type of white blood cell, thereby weakening the immune response.

Muscular and Joint Pain

Stress may intensify chronic pain caused by arthritis and other conditions. Psychological distress also plays a significant role in the severity of back pain. Some studies have clearly associated job dissatisfaction and depression to back problems, although it is still unclear whether stress is a direct cause of the back pain. Research suggests that the risk of developing long-term disability from low back pain can be reduced through early treatment of depression and stress.

Headaches

Tension-type headaches are highly associated with stress and stressful events. Sometimes the headache does not start until long after the stressful event has ended. Additionally, stress can contribute to the development or cause headaches to occur more frequently.

Some research suggests that people who experience tension-type headaches may have some biological predisposition for translating stress into muscle contractions. Among the wide range of possible migraine triggers is emotional stress, although the headaches often erupt after the stress has eased.

Sleep Disturbances

The tensions of unresolved stress frequently cause insomnia, which prevents stressed people from sleeping or causes them to awaken in the middle of the night or early morning. This appears to be due to the fact that stress causes physiological arousal during non-rapid eye movement sleep.

Sexual and Reproductive Dysfunction

Sexual Function

Stress can reduce sexual desire and lead to sexual dysfunction in both women and men.

Premenstrual Syndrome

Some studies indicate that the stress response in women with premenstrual syndrome may be more intense than in those without the syndrome.

Fertility

Chronic stress may affect fertility. Stress hormones have an impact on the hypothalamus, which produces reproductive hormones. This effect may lead to changes in a woman's menstrual cycle, as well as a reduction in a man's sperm count. Stress can also reduce sex drive.

Effects on Pregnancy

Stress may cause physiological alterations, such as increased adrenal hormone levels or resistance in the arteries, which may interfere with normal blood flow to the placenta. Maternal stress during pregnancy has been linked to a higher risk for miscarriage, lower birth weight, and an increased incidence of premature births. Some evidence also suggests that an expectant mother's stress can even influence the way in which her baby's brain and nervous system will react to stressful events. One study found a higher rate of crying and lower attention in infants of mothers who had been stressed during pregnancy. Other studies linked maternal stress to a higher risk of the child for cardiovascular disease later in life.

Menopause

A drop in estrogen levels during perimenopause and menopause may be responsible for changes in mood precipitated by stress.

Memory, Concentration, and Learning

Stress affects the brain, particularly memory, but the effects vary widely depending on whether the stress is acute or chronic.

Effect of Acute Stress on Memory and Concentration

Studies indicate that the immediate effect of acute stress impairs short-term memory, particularly verbal memory. On the plus side, high levels of stress hormones during short-term stress have been associated with enhanced memory storage, improved working memory, and greater concentration on immediate events. The difference in effect may be due to how cortisol impacts glucocorticoid receptors in the hippocampus and prefrontal cortex.

Effect of Chronic Stress on Memory

If stress becomes chronic, sufferers often lose concentration at work and home, and they may become inefficient and accident-prone. In children, the physiologic responses to chronic stress can interfere with learning. Studies have connected long-term exposure to excess amounts of the stress hormone cortisol to a shrinking of the hippocampus, the brain's memory center. It is not yet known whether this shrinking is reversible.

Other Disorders

Skin Disorders

Stress may worsen numerous skin conditions, including hives, psoriasis, acne, and rosacea, and it is one of the most common causes of eczema. Unexplained itching may also be caused by stress. Evidence suggests that experiencing the stress of a traumatic event (parental divorce or separation, or a severe disease in a family member) before age 2 increases the risk of developing eczema.

Unexplained Hair Loss (Alopecia Areata)

Alopecia areata is hair loss that occurs in localized (individual) patches. The cause is unknown, but stress is suspected as a player in this condition. For example, hair loss often occurs during periods of intense stress, such as when people are in mourning.

Teeth and Gums

Stress has now been implicated in increasing the risk for periodontal disease, which can cause tooth loss and has been linked to heart disease.

Substance Abuse

People who are under chronic stress may turn to alcohol or drug use for relief. Stress compounds the damage that these destructive habits cause under ordinary circumstances. Many people also resort to unhealthy eating habits, smoking, or passive activities, such as watching television when they are stressed.

Alcohol affects receptors in the brain that reduce stress. Lack of nicotine increases stress in smokers, which creates a cycle of dependency on smoking.

The cycle is self-perpetuating: a sedentary routine, an unhealthy diet, alcohol or drug abuse, and smoking all promote heart disease. They also interfere with sleep patterns, and lead to increased rather than reduced tension levels. Drinking 4 or 5 cups of coffee, for example, can cause changes in blood pressure and stress hormone levels similar to those produced by chronic stress. Unhealthy diets high in animal fats, simple sugars, and salt are known contributors to health problems.

Conditions with Similar Symptoms

The physical symptoms of anxiety disorders mirror many symptoms of stress, including:

- A fast heart rate
- Rapid, shallow breathing
- Increased muscle tension

Anxiety is an emotional disorder that is characterized by feelings of apprehension, uncertainty, fear, or panic. Unlike stress, the triggers for anxiety are not usually associated with specific stressful or threatening conditions. Some individuals with anxiety disorders have numerous physical complaints, such as headaches, gastrointestinal disturbances, dizziness, and chest pain. Severe cases of anxiety disorders are debilitating, interfering with a person's career, family, and social life.

Depression

Depression can be a disabling condition, and, like anxiety disorders, it may sometimes be linked to chronic stress. Individuals with high levels of work-related stress are more than twice as likely to experience a major depressive episode, compared with people who are under less stress. Evidence also suggests that certain people may be genetically susceptible to depression after they experience stressful life events.

Depression shares some of the symptoms of stress, including changes in appetite, sleep patterns, and concentration. Serious depression, however, is distinguished from stress by feelings of sadness, hopelessness, loss of interest in life, and, sometimes, thoughts of suicide. Acute depression is also accompanied by significant changes in the person's functioning. The person may need professional therapy to determine whether depression is caused by stress, or if it is the primary problem.

Post-Traumatic Stress Disorder Symptoms

Post-traumatic stress disorder (PTSD) is a reaction to a very traumatic event. The event that brings on PTSD is usually outside the norm of human experience, such as intense combat or sexual assault. The patient struggles to forget the traumatic event and frequently develops emotional numbness and event-related amnesia. Often, however, there is a mental flashback, and the person re-experiences the painful circumstance in the form of dreams and disturbing thoughts and memories. These thoughts and dreams resemble or recall the trauma. Other symptoms may include a lack of pleasure in previously enjoyed activities, hopelessness, irritability, mood swings, sleep problems, inability to concentrate, and an excessive startle-response to noise.

There are several screening tools available to screen for post-traumatic stress, such as Breslau Short Screening Scale and Primary Care PTSD Screen (PC-PTSD).

While various interventions to treat or prevent PTSD are being tested, not just one program will help all victims, and research is somewhat limited. Many experts favor a multifactorial approach to therapy that includes talk therapy such as cognitive-behavioral therapy (CBT) and medications such as selective serotonin reuptake inhibitors (SSRIs). Core symptoms of PTSD can be treated with medications. For example, prazosin is effective for treating trauma nightmares associated with PTSD.

There is evidence that CBT is effective in treating children and adolescents with PTSD, but more research is needed.

Early intervention appears to have the most benefit.

Acceptance and commitment therapy (ACT) is another form of behavioral therapy being evaluated for treating PTSD.

On the horizon are "virtual therapies," computerized programs or simulations, to treat PTSD symptoms. This approach is being studied in military veterans suffering from PTSD.

Treatment

The process of learning to control stress is life-long. Overcoming stress will not only contribute to better health, but it will also increase an individual's ability to succeed.

When to Seek Professional Help for Stress

Stress can be a factor in a variety of physical and emotional illnesses, which should be professionally treated. Many stress symptoms are mild and can be managed with over-the-counter medications (for example, aspirin, acetaminophen, or ibuprofen for tension headaches; antacids, anti-diarrhea medications, or laxatives for mild stomach distress). A physician should be consulted, however, for physical symptoms that are out of the ordinary, particularly those that get worse or wake a person up at night. A mental health professional should be consulted for unmanageable acute stress or for severe anxiety or depression. Often short-term therapy can resolve stress-related emotional problems.

The Depression Anxiety Stress Scales (DASS) and other assessment tools are available to help identify aspects of stress such as difficulty relaxing, nervous arousal and being agitated/irritable, and determine whether depression and/or anxiety are present as well. The DASS is available to the public online.

Considerations for Choosing a Stress-Reduction Strategy

When choosing specific strategies for treating stress, several factors should be considered.

- **No single method is always successful.** A combination of approaches is generally most effective.
- **What works for one person does not necessarily work for someone else.**
- **Stress can be positive as well as negative.** Appropriate and controllable stress provides interest and excitement and motivates the individual to greater achievement. A lack of stress may lead to boredom and depression.

Stress may play a part in making people vulnerable to illness. A physician or psychologist should be consulted if there are any indications of accompanying medical or psychological conditions, such as heart symptoms, significant pain, anxiety, or depression.

Overcoming Obstacles to Treatment

People often succeed in relieving stress for the short term. However, they go back to their previous stressful thoughts and behaviors because of outside pressure, long-held beliefs, or old habits. The following are some obstacles to managing stress:

- **The fight or flight urge.** The very idea of relaxation can feel threatening because it is perceived as letting down one's guard. For example, an over-demanding boss may put a subordinate into a psychological state of fighting-readiness, even though there is no safe opportunity for the subordinate to fight back or express anger. Stress builds up, but the worker has the illusion, even subconsciously, that the stress itself is providing safety or preparedness. For this reason, the employee does nothing to correct the condition.

- Many people are afraid of being perceived as selfish if they engage in stress-reducing activities that benefit only themselves. The truth is that self-sacrifice (not intended for reducing one's stress) may be inappropriate and even damaging, if the person making the sacrifice is unhappy, angry, or physically unwell.
- Some people believe that certain emotional responses to stress, such as anger, are natural and unchangeable features of their personality. Research has shown, however, that with cognitive behavioral therapy, individuals can be taught to change their emotional reactions to stressful events.
- In addition, many Americans report that lack of willpower, time, finances, and stress itself are barriers to better stress management.

Reducing stress and staying relaxed clears the mind so it can begin the appropriate actions to get rid of the stress-related conditions.

Stress Reduction and Its Effects on Health

Although treating stress cannot cure medical problems, stress management can be a very important part of medical treatment. Specific stress reduction approaches may benefit different medical problems. For example, relaxation methods may help people with high blood pressure. Stress reduction may improve well-being and quality of life in many people who are experiencing stress because of severe or chronic medical conditions.

Important Note: Never use stress reduction techniques as the only treatment, or in place of proven treatments, for any medical condition.

Lifestyle Changes

A healthy lifestyle is an essential companion to any stress-reduction program. People can enhance their general health and stress resistance by getting regular exercise, eating a diet rich in a variety of whole grains, vegetables, and fruits, and avoiding excessive alcohol, caffeine, and tobacco.

Exercise

Exercise in combination with stress management techniques is extremely important for many reasons:

- Exercise is an effective distraction from stressful events.
- Exercise may directly blunt the harmful effects of stress on blood pressure and the heart (exercise protects the heart).

Vary the exercise program, combining aerobic exercise with strength training. Start slowly. Strenuous exercise in people who are not used to it can be very dangerous. In addition, one-half of all people who begin a vigorous training program drop out within a year. Discuss any exercise program with a health care provider before starting. The key is to find activities that are exciting, challenging, and satisfying. The following are some suggestions:

- Aerobics classes at a gym
- Brisk walking (even short walks can relieve bouts of stress) or running
- Swimming (an ideal exercise for many stressed people, including pregnant women, people with musculoskeletal problems, and those who have exercise-induced asthma)
- Yoga or Tai chi (these techniques combine many of the relaxation benefits of breathing, muscle relaxation, and meditation while toning and stretching the muscles)

As in other areas of stress management, making a plan and executing it successfully provides feelings of mastery and control, which are very beneficial in and of themselves. Start slowly. Just 10 minutes of exercise 3 times a week can build a good base for novices. Gradually build up the length of these sessions to 30 minutes or more.

Cognitive-Behavioral Therapy

Cognitive-behavioral therapy (CBT) is among the most effective ways of reducing stress, whether the source of stress is chronic pain or a chronic disease. CBT may be more helpful than support groups for improving well-being and quality-of-life. It aims to alter behavior and change thoughts, feelings, and beliefs.

A typical CBT approach includes identifying sources of stress, restructuring priorities, changing one's response to stress, and finding methods for managing and reducing stress.

Identifying Sources of Stress

One key component in most CBT approaches is keeping a diary to record daily events and activities. The first step is to note activities that put a strain on energy and time, trigger anger or anxiety, or precipitate a negative physical response (such as a sour stomach or headache). Also note positive experiences, such as those that are mentally or physically refreshing or that produce a sense of accomplishment.

After a week or 2, try to identify 2 or 3 events or activities that have been significantly upsetting or overwhelming.

Questioning the Sources of Stress

Individuals should then ask themselves the following questions:

- Do these stressful activities meet my goals or someone else's?
- Have I taken on tasks that I can reasonably accomplish?
- Which tasks are under my control and which ones aren't?

Restructuring Priorities

Adding Stress Reducing Activities

The next step is to attempt to shift the balance from stress-producing to stress-reducing activities. Eliminating stress entirely is rarely possible, but there are many ways to reduce its impact.

Consider as many relief options as possible. Examples include:

- **Listen to music.** Music is an effective stress reducer in both healthy individuals and people with health problems. Research finds that listening to soothing music can decrease blood pressure, heart rate, and anxiety levels in heart patients.
- **Take long weekends or vacations.**
- **If the source of stress is in the home, plan times away, even if only for an hour or two a week.**
- **Replace unnecessary time-consuming chores with pleasurable or interesting activities.**
- **Make time for recreation.** This is as essential as paying bills or shopping for groceries.
- **Own a pet.** Research finds that pet owners have a lower blood pressure increase in response to stress than people who do not own pets.

Discuss Feelings

The concept of communication and letting your feelings out has been so excessively promoted and parodied that it has nearly lost its value as good psychological advice. Nevertheless, feelings of anger or frustration that are not expressed in an acceptable way may lead to hostility, a sense of helplessness, and depression.

Expressing feelings does not mean venting frustration. In fact, anger may cause a spike in blood pressure in some people. Some therapists strongly recommend just talking, rather than venting anger.

The primary goal is to explain and assert one's needs to a trusted individual in as positive a way as possible. Direct communication may not even be necessary. Writing in a journal, writing a poem, or composing a letter that is never mailed may be sufficient.

Expressing one's feelings solves only one half of the communication puzzle. Learning to listen, empathize, and respond to others with understanding is just as important for maintaining the strong relationships necessary for emotional fulfillment and reduced stress.

Keep Perspective and Look for the Positive

Reversing negative ideas and learning to focus on positive outcomes helps reduce tension and achieve goals. The following steps, using an example of a person who is alarmed at the prospect of giving a speech, may be useful:

- First, identify the worst possible outcomes (forgetting the speech, stumbling over words, humiliation, and audience contempt).
- Rate the likelihood of these bad outcomes happening (probably very low, or the speaker would not have been selected in the first place).
- Envision a favorable result (a well-rounded, articulate presentation with rewarding applause).
- Develop a specific plan to achieve a positive outcome such as preparing in front of a mirror, using a video camera or tape recorder, or doing relaxation exercises.
- Try to recall previous situations that initially seemed negative but ended well.

Use Humor

Research has shown that humor is a very effective mechanism for coping with acute stress. Keeping a sense of humor during difficult situations is a common recommendation of stress management experts. Laughter not only releases the tension of pent-up feelings and helps a person maintain perspective, but it also appears to have actual physical effects that reduce stress hormone levels. It is not uncommon for people to laugh intensely during tragic events, such as the death of a loved one, because this laughter helps them endure the emotional pain of the experience.

Acceptance and Commitment Therapy (ACT)

ACT is another type of behavioral analysis and therapy used for a range of mental health issues, including stress. It employs acceptance and mindfulness strategies to help individuals cope with stress. Rather than try to change difficult thoughts and feelings and eliminate stress, as CBT does, ACT aims to help people adopt acceptance, mindfulness, cognitive witnessing, values, and committed action. The practice may help to alter the experience of stress. ACT is based on six core practices:

- Acceptance of odd or uncomfortable thoughts, feelings, and sensations
- Observing one's own uncomfortable thoughts without automatically taking them literally or attaching too much significance to them
- Deciding to give attention to the present events rather than automatically focusing on the past or future
- A sense of self and ongoing awareness
- Identifying values that are personally important
- Commitment to action for achieving the personal values

ACT training can be delivered in one on one or group sessions, workshops, or self-help tools.

Relaxation and Other Alternative Techniques

Relaxation Method

Because stress is here to stay, everyone needs to develop methods to promote the relaxation response, the natural unwinding of the stress response. Relaxation lowers blood pressure, respiration, and pulse rate, releases muscle tension, and eases emotional strain. This response is highly individualized, but there are certain approaches that seem to work for most people. Meditation during the run-up to a stressful event can reduce the stress response without impairing alertness, concentration or memory.

Combinations of these techniques probably work best. No one should expect these approaches to completely relieve their stress, but if they are done regularly, these programs can be very effective. In a recent review, it was shown that mindfulness based stress reduction (MBSR) techniques are effective stress reliever, lowering stress in healthy people. Techniques include yoga and meditation. Significant reductions in stress levels were seen in participants compared to those not engaging in any treatment. Outcomes were assessed using the Mindfulness Attention Awareness Scale (MAAS).

Relaxation Methods	Specific Procedure
<p>Deep Breathing Exercises</p> <p>During stress, breathing becomes shallow and rapid. Taking a deep breath is an automatic and effective technique for winding down. Deep breathing exercises consciously intensify this natural physiologic reaction and can be very useful during a stressful situation, or for maintaining a relaxed state during the day.</p>	<ul style="list-style-type: none"> • Inhale through the nose slowly and deeply to the count of 10. • Make sure that the stomach and abdomen expand, but the chest does not rise. • Exhale through the nose, slowly and completely, also to the count of 10. • To help quiet the mind, concentrate fully on breathing and counting through each cycle. • Repeat 5 to 10 times, and make a habit of doing the exercise several times each day, even when not feeling stressed.
<p>Muscle Relaxation</p> <p>Muscle relaxation techniques, often combined with deep breathing, are simple to learn and very useful for getting to sleep. In the beginning, it is useful to have a friend or partner check for tension by lifting an arm and dropping it. The arm should fall freely. Practice makes the exercise much more effective and produces relaxation much more rapidly. Small studies have reported beneficial effects on blood pressure in patients with high blood pressure who use this technique.</p>	<ul style="list-style-type: none"> • After lying down in a comfortable position without crossing the limbs, concentrate on each part of the body. • Maintain a slow, deep breathing pattern throughout this exercise. • Tense each muscle as tightly as possible for a count of 5 to 10, and then release it completely. • Experience the muscle as totally relaxed and lead-heavy. • Begin with the top of the head and progress downward to focus on all the muscles in the body. • Be sure to include the forehead, ears, eyes, mouth, neck, shoulders, arms and hands,

fingers, chest, belly, thighs, calves, and feet.

- Once the review is complete, imagine tensing and releasing the internal muscles.

Meditation

Meditation, used for many years in Eastern cultures, is now widely accepted in the United States as a relaxation technique. The goal of all meditative procedures, both religious and therapeutic, is to quiet the mind (essentially, to relax thought). Small studies have suggested that regular meditation can benefit the heart and help reduce blood pressure. Better research is needed, however, to confirm such claims.

Some experts recommend meditating for no longer than 20 minutes in the morning after waking up and then again in the early evening before dinner. Even meditating just once a day is helpful.

New practitioners should understand that it can be difficult to quiet the mind, and should not be discouraged by a lack of immediate results.

Several techniques are available. A few are discussed here.

The only potential risks from meditating are in people with psychosis, in whom meditating may trigger a psychotic event.

Mindfulness Meditation

Mindfulness is a common practice that focuses on breathing. It employs the basic technique used in other forms of meditation.

- Sit upright with the spine straight, either cross-legged or sitting on a firm chair with both feet on the floor, uncrossed.
- With the eyes closed or gently looking a few feet ahead, observe the exhalation of the breath.
- As the mind wanders, simply note it as a fact and return to the "out" breath. It may be helpful to imagine the thoughts as clouds dissipating away.

Transcendental Meditation (TM)

TM uses a mantra (a word that has a specific chanting sound but no meaning). The person meditating repeats the word silently, letting thoughts come and go.

Mini-Meditation

The method involves heightening awareness of the immediate surrounding environment. Choose a routine activity, for example:

- While washing dishes, concentrate on the feel of the water and dishes.
- Allow the mind to wander to any immediate sensory experience (sounds outside the window, smells from the stove, colors in the room).
- If the mind begins to think about the past or future, or fills with unformed thoughts or worries, redirect it gently back.

	<ul style="list-style-type: none"> • This redirection of brain activity from your thoughts and worries to your senses disrupts the stress response and prompts relaxation. It also helps promote an emotional and sensual appreciation of simple pleasures.
<p>Biofeedback</p> <p>Biofeedback is a technique that measures bodily functions, such as breathing, heart rate, blood pressure, skin temperature, and muscle tension. By watching these measurements, individuals can learn how to alter these functions by relaxing or holding pleasant images in their mind.</p>	<ul style="list-style-type: none"> • During biofeedback, electric leads are taped to a subject's head. • The person is encouraged to relax using methods such as those described above. • Brain waves are measured and an audible signal is emitted when alpha waves are detected, a frequency that coincides with a state of deep relaxation. • By repeating the process, people associate the sound with the relaxed state and learn to achieve relaxation by themselves.
<p>Massage Therapy</p> <p>Massage therapy may decrease cortisol levels, and some research suggests a possible role of physical touch in managing stress.</p>	<p>Many massage techniques are available, such as the following:</p> <p>Swedish massage is the standard massage technique. It uses long smooth strokes, and kneading and tapping of the muscles.</p> <p>Shiatsu applies intense pressure to the same points targeted in acupuncture. It can be painful, but people report deep relaxation afterward.</p> <p>Reflexology manipulates acupuncture points in the hands and feet.</p>

Herbal and Natural Remedies

Some people who experience chronic stress try herbal or natural remedies. Although many benefits are claimed, few or none have been proven. Generally, manufacturers of herbal remedies and dietary supplements do not need FDA approval to sell their products. Just like drugs, however, herbs and supplements can affect the body's chemistry, and therefore have the potential to produce side effects that may be harmful. There have been numerous reported cases of serious and even lethal side

effects from herbal products. Always check with your doctor before using any herbal remedies or dietary supplements.

Aromatherapy

The smell of lavender has long been associated with a calming effect. In addition, several other aromatherapies are now used for relaxation. Use caution, however, as some of the exotic plant extracts in these formulas have been associated with a wide range of skin allergies. Aromatherapy products and essential oils should never be ingested.

Special Warning on Kava

Kava has been commonly used to reduce anxiety and stress. It is now highly associated with liver injury and even liver failure in a few cases. Experts now strongly warn against its use.

People seeking relief from stress should be wary of any product that promises a quick cure, or that requires the purchase of expensive treatments. These treatments may be useless and sometimes even dangerous.

Resources

- National Institute of Mental Health -- www.nimh.nih.gov
- National Alliance for the Mentally Ill -- www.nami.org
- Mental Health America (formerly the National Mental Health Association) -- www.mhanational.org
- The American Psychological Association -- www.apa.org
- American Academy of Child and Adolescent Psychiatry -- www.aacap.org
- The American Institute of Stress -- www.stress.org
- Depression Anxiety Stress Scale (DASS) -- www2.psy.unsw.edu.au/groups/dass

References

Åkerstedt T, Perski A, Kecklund G. Sleep, occupational stress, and burnout. In: Kryger M, Roth T, Dement WC, eds. *Principles and Practice of Sleep Medicine*. 6th ed. Philadelphia, PA: Elsevier; 2017:chap 77.

Arri SS, Ryan M, Redwood SR, Marber MS. Mental stress-induced myocardial ischaemia. *Heart*. 2016;102(6):472-480. PMID: 26729692 pubmed.ncbi.nlm.nih.gov/26729692/.

Bradt J, Dileo C, Potvin N. Music for stress and anxiety reduction in coronary heart disease patients. *Cochrane Database Syst Rev*. 2013;(12):CD006577. PMID: 24374731 pubmed.ncbi.nlm.nih.gov/24374731/.

Carpenter JK, Andrews LA, Witcraft SM, Powers MB, Smits JA, Hofmann SG. Cognitive behavioral therapy for anxiety and related disorders: a meta-analysis of randomized placebo-controlled trials. *Depress Anxiety*. 2018. PMID: 29451967 pubmed.ncbi.nlm.nih.gov/29451967/.

Drossman DA, Keefer L. Biopsychosocial issues in gastroenterology. In: Feldman M, Friedman LS, Brandt LJ, eds. *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*. 11th ed. Philadelphia, PA: Elsevier; 2021:chap 22.

Ferrie JE, Virtanen M, Jokela M, et al. Job insecurity and risk of diabetes: a meta-analysis of individual participant data. *CMAJ*. 2016;188(17-18):E447-E455. PMID: 27698195 pubmed.ncbi.nlm.nih.gov/27698195/.

Fuentes IM, Christianson JA. The influence of early life experience on visceral pain. *Front Syst Neurosci*. 2018;12:2. PMID: 29434541 pubmed.ncbi.nlm.nih.gov/29434541/.

- Gillies D, Maiocchi L, Bhandari AP, Taylor F, Gray C, O'Brien L. Psychological therapies for children and adolescents exposed to trauma. *Cochrane Database Syst Rev*. 2016;10:CD012371. PMID: 27726123 pubmed.ncbi.nlm.nih.gov/27726123/.
- Hackett RA, Steptoe A. Type 2 diabetes mellitus and psychological stress - a modifiable risk factor. *Nat Rev Endocrinol*. 2017;13(9):547-560. PMID: 28664919 pubmed.ncbi.nlm.nih.gov/28664919/.
- . Kivimäki M, Kawachi I. Work stress as a risk factor for cardiovascular disease. *Curr Cardiol Rep*. 2015;17(9):630. PMID: 26238744 pubmed.ncbi.nlm.nih.gov/26238744/.
- Kivimäki M, Jokela M, Nyberg ST, et al. Long working hours and risk of coronary heart disease and stroke: a systematic review and meta-analysis of published and unpublished data for 603,838 individuals. *Lancet*. 2015;386(10005):1739-1746. PMID: 26298822 pubmed.ncbi.nlm.nih.gov/26298822/.
- Ma H, Guo L, Huang D, et al. The role of the myocardial microvasculature in mental stress-induced myocardial ischemia. *Clin Cardiol*. 2016;39(4):234-239. PMID: 26895096 pubmed.ncbi.nlm.nih.gov/26895096/.
- Noordali F, Cumming J, Thompson JL. Effectiveness of mindfulness-based interventions on physiological and psychological complications in adults with diabetes: a systematic review. *J Health Psychol*. 2017;22(8):965-983. PMID: 26721631 pubmed.ncbi.nlm.nih.gov/26721631/.
- Pelliccia F, Kaski JC, Crea F, Camici PG. Pathophysiology of Takotsubo syndrome. *Circulation*. 2017;135(24):2426-2441. PMID: 28606950 pubmed.ncbi.nlm.nih.gov/28606950/.
- Schorr L, Burger A, Hochner H, et al. Mortality, cancer incidence, and survival in parents after bereavement. *Ann Epidemiol*. 2016;26(2):115-121. PMID: 26809234 pubmed.ncbi.nlm.nih.gov/26809234/.
- Vaccarino V, Bremner JD. Psychiatric and behavioral aspects of cardiovascular disease. In: Zipes DP, Libby P, Bonow RO, Mann DL, Tomaselli GF, Braunwald E, eds. *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*. 11th ed. Philadelphia, PA: Elsevier; 2019:chap 96.
- Wei J, Rooks C, Ramadan R, et al. Meta-analysis of mental stress-induced myocardial ischemia and subsequent cardiac events in patients with coronary artery disease. *Am J Cardiol*. 2014;114(2):187-192. PMID: 24856319 pubmed.ncbi.nlm.nih.gov/24856319/.
- Wirtz PH, von Känel R. Psychological stress, inflammation, and coronary heart disease. *Curr Cardiol Rep*. 2017;19(11):111. PMID: 28932967 pubmed.ncbi.nlm.nih.gov/28932967/.
- Wokhlu A, Pepine CJ. Mental stress and myocardial ischemia: young women at risk. *J Am Heart Assoc*. 2016;5(9). PMID: 27559073 pubmed.ncbi.nlm.nih.gov/27559073/.
- Younge JO, Gotink RA, Baena CP, Roos-Hesselink JW, Hunink MG. Mind-body practices for patients with cardiac disease: a systematic review and meta-analysis. *Eur J Prev Cardiol*. 2015;22(11):1385-1398. PMID: 25227551 pubmed.ncbi.nlm.nih.gov/25227551/.

Review Date: 7/20/2020

Reviewed By: Fred K. Berger, MD, addiction and forensic psychiatrist, Scripps Memorial Hospital, La Jolla, CA. Also reviewed by David Zieve, MD, MHA, Medical Director, Brenda Conaway, Editorial Director, and the A.D.A.M. Editorial team.