Adaptogens

Herbs for Strength, Stamina, and Stress Relief

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Part Three: Herbal Adaptogens in Use

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Adaptogens and the Stress Response

Health is the ability to adapt to one's environment.

Georges Canguilhem,
The Normal and the Pathological

Russian research in the 1950s and 1960s on eleuthero and other adaptogens concluded that they enhanced the body's ability to handle all types of stressors.

This chapter discusses how adaptogens help the body adapt to stress and support normal function from a biological and physiological perspective. It also discusses stress physiology and biomedical stress theory. Throughout the chapter explanations will range from simple to more complex; any unusual terminology will be clearly defined. Please view these details as additional reference material because it becomes somewhat technical.

Stress causes changes in hormone levels as well as immune system, cardiac, and gastrointestinal function. Prolonged stress results in predictable effects on the body, and the physiological and psychological consequences of acute and chronic stress can persist well beyond the actual ending of a stressful event.

Stress is also two-sided; a little bit is both good and necessary, but intense or chronic stress can be harmful. It is not exclusively connected to difficulties and unpleasant events. A state of stress can exist even while we are experiencing positive events. It is our body's reaction to changes in our environment and psyches.

The term *stress* also can be used in the negative sense of *distress* and can be used to describe a chronic state of imbalance in the response to stressful events.

Common Stressors

Biological: caused by exposure to bacteria, viruses, fungi, and parasites

Chemical: caused by exposure to toxins including pesticides, herbicides, fungicides, insecticides, heavy metals, household and industrial chemicals, fumes, xenoestrogens (foreign substances that imitate the effects of estrogen), dust, smoke, tobacco, and pharmaceutical drugs

Environmental: caused by exposure to extreme cold or heat, noise, ultraviolet sunlight, changes in barometric pressure or altitude, allergens, electromagnetic influences (microwaves, radio waves, high-voltage electric lines), and ionizing radiation

Nutritional: caused by food allergies, simple carbohydrates, highly processed foods, mineral-depleted food (grown in poor soil), nutritional deficiencies, alcohol, rancid fats and trans fats, artificial preservatives and food colors, processed meats, and grilled foods

Physical: caused by high blood pressure, strenuous physical activity including exercise, surgery, trauma, starvation, lack of oxygen, intoxication, drug use, sleep deprivation, severe illness, infection, being pregnant or having a new baby, and chronic overstimulation

Psychological: caused by depression, anger, fear, anxiety, worry, desire, grief, loss, mental illness, major change, mental trauma, and overwhelming responsibility; psychological stress frequently accompanies physical stress

Spiritual: caused by a sense of the loss of meaning in one's life and soul sickness

A stressor is any agent or event that threatens the body's normal homeostasis. Stressors are not uniform events with identical effects on neuroendocrine and immune function. It is difficult to know exactly how they will affect the various body systems. One stressor might lead to intense nervous system activation but have little effect on HPA axis hormonal responses, or the effect might be a blend of hormonal activity and nervous system activation. The impact of stressful events also depends on other factors such as a person's constitution, personality, and heredity as well as the intensity, severity, timing, and duration of the stressful conditions. All factors that are considered to be stressors strongly affect physiological and psychological function.

The Body's Response to Stress

Canadian endocrinologist Hans Selye, who is known as the father of stress research, said, "It is not stress that kills us, it is our reaction to it." Regulation of the stress response involves three primary systems of the body: the endocrine system, the central nervous system (particularly the autonomic nervous system, which controls unconscious functioning), and the immune system. The neuroendocrine system, specifically the HPA axis, is one of the body's major auto-regulatory systems. The effective functioning of all of these systems is important to our vitality and any dysregulation or disharmony can cause health problems and disease.

The process of reestablishing homeostasis that is disturbed by stressors is called the *adaptive response* because it enables the body to adapt to the influence of stressors.

Stress is managed by two different physiological systems: the *hypothalamic-pituitary-adrenal* (HPA) axis and the *sympathoadrenal system* (SAS), which is the interface between the sympathetic nervous system and adrenal glands. If the hypothalamus in the brain perceives something as stressful, it activates a cascade of hormones that are referred to as *stress-response hormones*. The body's stress system, the HPA and SAS, produces various changes in the body in response to the influence of stressors. These changes cause the body to adapt and strive to reestablish balance.

Adaptogens help the body achieve an adaptive response to stress; they increase the ability of the body to cope more effectively with stress. They work to modify the body's reaction to stress and alter the release of stress hormones in the body.

When the body is under stress, it is using more energy. The body's energy supply is being depleted more quickly because vital nutrients are being converted to energy. This can cause fatigue if the process goes on for too long and can lead to a variety of health problems.

Another effect of normal metabolism is the creation of proinflammatory reactive oxygen and nitrogen species (ROS, RNS), commonly known as free radicals. If the concentration of free radicals exceeds the body's capacity to neutralize them, then cells can be harmed—especially mitochondria, the cell's "engine." These compounds are quenched by cellular antioxidants such as superoxide dismutase (SOD), catalase, and reduced glutathione. Adaptogens have been shown to stimulate cellular and organism defense systems and enhance survival against oxidative stress (Panossian et al. 2017).

Physiological Description of the Stress Response

Stress is perceived by the limbic system within the brain. Almost immediately after a stressful event, neurons activate the HPA axis and the SAS, which releases various hormones that are filtered through the HPA axis and travel through the tissues and bloodstream. In the hypothalamus, stressors stimulate the release of corticotropin-releasing hormone (CRH). Then, CRH travels to the pituitary gland, where it triggers the release of adrenocorticotropic hormone (ACTH). Next, ACTH triggers the production and release of hormones called glucocorticoids (GCs), primarily cortisol, from the adrenal cortex. The hypothalamus also stimulates the adrenal gland, via the sympathetic nervous system, to release catecholamines, such as adrenaline (epinephrine) and noradrenaline (norepinephrine), into the bloodstream. The combination of the release of adrenaline and noradrenaline results in the well-known fight-or-flight response. Catecholamines and GCs induce a variety of behavioral, biochemical, and physiological changes, collectively termed the *stress response*. This response will be discussed in the following sections.

Neuroendocrine System

The endocrine system and the nervous system are so closely associated that they are collectively called the *neuroendocrine system*. The hypothalamus and pituitary gland form a complex interface between the nervous and endocrine systems. The brain can influence the activity of nerve cells, which signal the adrenal system to release hormones that can influence the release of other hormones. The neuroendocrine system is complex. This overview will touch on the aspects that affect the stress response. It will also provide definitions of the major components and hormones involved within the neuroendocrine and immune systems.

The HPA axis plays an essential role in the body's response to stress and plays a central role in the function of the neuroendocrine system.

Limbic system is a collective term denoting brain structures (including the hippocampus) and interconnections of these structures. The limbic system exerts an important influence upon the neuroendocrine system.

Endocrine System

The endocrine system is composed of glands that release their hormones directly into the bloodstream to send chemical signals to target cells. These glands include the pituitary gland, pineal gland, hypothalamus, thyroid gland, parathyroid glands, thymus, adrenal glands, ovaries (in females) or testes (in males), and islets of Langerhans in the pancreas.

The main neural control center in the brain is the hypothalamus, also known as the "keeper of internal balance" or the "master switchboard." The hypothalamus secretes hormones that cause other endocrine glands to secrete hormones. It directs the fight-or-flight response of the autonomic nervous system. Its main function is homeostasis, or maintaining the body's balance. The bodily functions that it regulates include blood pressure, body temperature, fluids and electrolytes, and body weight.

The hypothalamus has two main outputs to signal stress response: endocrine signals to the pituitary and adrenal glands and neural signals to the sympathetic nervous system, including signals to the medulla of the adrenal gland.

The hypothalamus can control every endocrine gland in the body and can alter blood pressure, body temperature, metabolism, and adrenaline levels. If the hypothalamus perceives something as stressful, it activates hormones to initiate the stress response.

The pituitary gland is suspended from the hypothalamus by a thin stalk. It is sometimes called the "master gland" because it regulates many crucial functions. The pituitary gland produces and secretes hormones in response to commands from the hypothalamus. Structurally, the pituitary gland is divided into two parts, the anterior and posterior lobes, each having separate functions. The anterior lobe regulates the activity of the thyroid and adrenal glands as well as the reproductive glands. The posterior lobe (neurohypophysis) secretes two hormones: oxytocin, a peptide hormone, and antidiuretic hormone, also known as vasopressin.

The adrenal glands are on top of each kidney. Each gland has a cortex (outer region) and a medulla (inner region). The adrenals handle the stress response by producing hormones and stimulating the sympathetic nervous system. Adrenaline (epinephrine) and noradrenaline (norepinephrine) are secreted from the adrenal medulla in response to sympathetic nervous system stimulation. Cortisol is secreted from the adrenal cortex in response to HPA stimulation.

Autonomic Nervous System

The autonomic nervous system is the part of the overall nervous system that controls involuntary bodily functions. Its name comes from the term *autonomous,* and it runs bodily functions that are beyond our awareness or control. It regulates, via the nerves, the functions of glands, smooth muscle tissue, and cardiac muscle. It consists of two physiologically and anatomically distinct, mutually antagonistic components: the sympathetic nervous system and the parasympathetic nervous system. The two subdivisions function in a dynamic balance aiming at homeostasis.

The sympathetic nervous system is the part of the autonomic nervous system that is active during stress and is a central regulatory system that assists in maintaining homeostasis. It specifically includes nerve cells involved in the stress response (the fight-or-flight response).

The parasympathetic nervous system has many specific functions, including slowing the heart, stimulating the gut and salivary glands, and other responses that are not a priority during stressful situations. As the sympathetic nervous system is active during stress, the parasympathetic system remains calm, recharges the body, and tries to keep things balanced. The state of the body at any given time represents a balance between the sympathetic and parasympathetic systems.

Sympathoadrenal System

The interface between the hypothalamus, adrenal medulla, and sympathetic nervous system is referred to as the *sympathoadrenal system* (SAS). This system creates the fight-or-flight response that controls the body's reaction to a stressor, resulting in increased levels of adrenaline and other chemicals.

The fight-or-flight response can be set off by one or more stressors and triggers a wide array of physical responses. These include an increase in mental focus, heart rate, respiration, blood flow, blood sugar levels, oxygen consumption, and nervous system activity. The response also triggers a decrease in digestive function and the release of adrenaline and/or noradrenaline into the bloodstream. Under severe stress, men stop producing sperm and hair and women stop producing reproductive hormones and start to store fat. This response also has been called *fright-flight-or-fight.*

Stress Hormones

The following section describes the different hormones secreted by the endocrine system and how they relate to the body's stress response.

Table 5.1. Endocrine System Hormones

ENDOCRINE GLAND	HORMONE
Hypothalamus	Corticotropin-releasing hormone (CRH)
Anterior pituitary	Thyroid-stimulating hormone (TSH), also known as thyrotropin; Adrenocorticotropic hormone (ACTH); and growth hormone (GH)
Posterior pituitary	Vasopressin and oxytocin
Adrenal cortex	Cortisol or hydrocortisone (glucocorticoid) Dehydroepiandrosterone (DHEA) Aldosterone (mineralocorticoid) Adrenosterone or andrenosterone (adrenal androgen)
Adrenal medulla	Adrenaline or epinephrine (catecholamine) Noradrenaline or norepinephrine

Cortisol

Cortisol (hydrocortisone) is the hormone released from the adrenal glands in response to stress; it is often called the "stress hormone." It is the most potent of the naturally occurring glucocorticoids and is essential to metabolism as well as the stress response.

Cortisol secretion increases in response to any stress in the body, whether it is physical or psychological. When cortisol is secreted, it causes a breakdown of muscle protein, leading to the release of amino acids (the "building blocks" of protein) into the bloodstream. These amino acids then are used by the liver to synthesize glucose for energy, in a process called *gluconeogenesis*. This process raises the blood sugar level so the brain will have more glucose for energy. At the same time, the other tissues of the body decrease their use of glucose as fuel. Cortisol secretion also leads to the release of fatty acids for use by the muscles. Taken together, these processes that direct and replenish energy prepare the body to deal with stress and ensure that the brain receives adequate energy sources. Cortisol's other important functions in the body are the regulation of blood pressure and cardiovascular function as well as helping the immune system respond to infection and inflammation. Cortisol levels in normal individuals are highest at around six to eight in the morning and are lowest around midnight.

Too much cortisol can suppress immune function and interfere with sleep, digestion, sex hormone balance, and circulation. Symptoms of elevated cortisol can include anxiety, hypertension, sex hormone imbalance, insulin resistance, obesity, osteoporosis, insomnia, and polycystic ovary syndrome (in women).

Too little cortisol can cause inflammatory disease. Symptoms of depressed cortisol can include Addison's disease, depression, chronic fatigue syndrome, hypotension, insomnia, premenstrual syndrome (PMS, in women), infertility, impotence (in men), and fibromyalgia.

Other Stress Hormones

Adrenocorticotropic hormone (ACTH, also known as corticotropin) is a hormone secreted by the anterior part of the pituitary gland. Levels of this hormone increase in response to stress, disease, and decreased blood pressure. The specific function of ACTH is to stimulate the growth and secretions of the cortex (outer layer) of the adrenal gland. These secretions include corticoids (also known as corticosteroids). Among the corticoids are the glucocorticoids, including cortisol.

Catecholamines (adrenaline, noradrenaline) are released by the adrenal medulla and affect the sympathetic nervous system. They produce widespread effects throughout the body, including an increase in blood pressure and heart rate during times of stress.

Adrenaline (epinephrine) is normally present in the bloodstream in minute quantities. In times of excitement or stress, additional quantities are secreted, causing an effect on body structures in preparation for physical exertion (either fight or flight). Adrenaline stimulates the heart, facilitates blood flow to muscles and the brain, constricts the small blood vessels, raises blood pressure, liberates sugar stored in the liver, and relaxes certain involuntary muscles while contracting others.

Noradrenaline (norepinephrine) is chemically related to adrenaline. It helps maintain normal blood circulation and can increase blood pressure. It is also the chemical agent responsible for the transmission of nerve impulses in the autonomic nervous system.

Thyroid-stimulating hormone (TSH) is secreted by the pituitary gland and stimulates the thyroid gland to secrete hormones (T3 and T4) that affect metabolic function.

Dehydroepiandrosterone (DHEA) is an androgenic steroid hormone produced by the adrenal cortex. Its primary function is to inhibit the binding of cortisol. It is a functional antagonist of cortisol. Cortisol and DHEA levels serve as good indicators of HPA axis activity. When cortisol levels go up, DHEA drops, and when DHEA levels are normal, cortisol also normalizes. Low DHEA levels can weaken the immune system.

Corticotropin-releasing hormone (CRH) is the hormone released from the hypothalamus that interacts with the pituitary to produce ACTH.

Aldosterone is a hormone produced by the adrenal cortex that affects the kidneys and blood pressure by its regulation of sodium, potassium, and fluid volume in the body.

In addition to the stress hormones, there are feedback controls that are set into motion following an increase in stress hormones, eventually signaling the hypothalamus to stop producing its messenger CRH hormone.

Adaptogens and the Neuroendocrine System

Adaptogenic herbs support the entire neuroendocrine system, and in particular adrenal function, thus counteracting the adverse effects of stress. Adaptogens also help the body with its natural adaptive responses to stress. They do this by exerting a biochemical influence on the hypothalamus and its two main systems to signal stress response—the HPA axis and the SAS.

The stress response pathways are as follows:

HPA: Stressor → hypothalamus → CRH → pituitary → ACTH → adrenal cortex → cortisol (to mobilize energy)

SAS: Stressor → hypothalamus → sympathetic nervous system → adrenal medulla → adrenaline (prepares the body for the fight-or-flight response)

Adaptogens help modulate and regulate the production of cortisol, allowing the body to maintain a healthy stress response. They also help regulate and support the interconnected neuroendocrine and immune systems, allowing the body to maintain optimal homeostasis.

Immune System

The immune system is a network of specialized cells, tissues, and organs that protect the body from pathogens (disease-causing agents) such as bacteria, viruses, fungi, and tumors. It includes the lymph nodes, lymphatic vessels, Peyer's patches, gut-associated lymphoid tissue (GALT), bone marrow, spleen, tonsils, thymus, and the intestinal microbiome. Normal functioning of the immune system is critical to our health and resistance to infection. Immunity is an expression of homeostasis within the immune system.

When pathogens invade the body, the immune system launches a nonspecific response through antibody and cellular actions. It begins with inflammation, which is increased blood flow to the affected area. Inflammation signals chemical messengers to send white blood cells to destroy invading pathogens. When the immune system is functioning properly, it can protect the body against many pathogens.

The neuroendocrine system works in concert with the immune system, communicating via neurotransmitters, which are substances that send signals between nerve cells, and hormones that travel through the tissues and the bloodstream. They interact to maintain homeostasis, even while a person is under acute or chronic stress.

The release of stress hormones involves a negative feedback system to inhibit continued release of cortisol and other hormones. This feedback system temporarily suppresses the immune system and also can reduce the number of beneficial white blood cells that protect the body.

Researchers have found that the brain is a dominant player that controls a great deal of immune system function (the gut/enteric brain and intestinal microbiome are also key players in healthy immune system function). Yet they also found that the cells of the immune system can communicate among themselves and that interleukins can interact with nerve cells, thereby creating a link between the immune system and the nervous system. As discussed in chapter 4, the study of psychoneuroimmunology is a relatively new science that is helping us better understand how the mind and immune systems interact to impair or improve our health.

Other Immune System Components

Lymphocytes are white blood cells formed in lymphatic tissue (lymph nodes, spleen, thymus, bone marrow). The two main classes of lymphocytes that are responsible for producing the immune response are the B cells and T cells. B cells ("B" for bone marrow) grow to maturity in the bone marrow, and T cells ("T" for thymus) mature in the thymus. The lymphatic system is composed of vascular channels that transport varying numbers of white blood cells (chiefly lymphocytes) throughout the body.

Lymphocytes react to antigens, which are substances released by invading pathogens. To fight pathogens, B cells release antibodies, proteins that attach to antigens, keeping them from harming the body.

Cytokines (including interleukins and interferon) are proteins (peptides) produced by white blood cells that act as chemical messengers between cells. They can stimulate or inhibit the growth and activity of various immune cells. Interleukins are chemicals found in leukocytes that stimulate them to fight infection. Interferon is a complex protein that is produced by cells in response to a virus (or bacteria) and inhibits virus development. Natural killer (NK) cells are lymphocytes that lack B-cell and T-cell receptors. They are designed to kill certain mutant and virus-infected cells. Helper cells activate the production of antibodies by B cells.

Stress and the Immune System

Chronic stress suppresses the ability of the immune system to do its job. This is in contrast to acute stress. The difference between acute (short-lived) stress and chronic (ongoing) stress must be recognized. The neuroendocrine system reacts to stress in seconds or minutes. The immune system can take hours or days to react. Short-lived stress can usually be dealt with and, as such, does not adversely affect the immune system.

When stress becomes chronic, then the immune system begins to be impaired. Cortisol from the adrenal glands adversely affects the immune system, decreasing the number of white blood cells. Accumulated or compounded stress over time can lead to a state of allostatic overload in which serious problems can result (see the discussion of allostasis beginning on page 93).

Any type of significant stress can have a detrimental effect on the ability to maintain optimal NK-cell activity. A severely stressful event can be associated with up to a 50 percent reduction of NK-cell function. Chronic stress preceding an acutely stressful event also significantly impacts NK-cell activity.

Adaptogens and the Immune System

Adaptogens have a focused effect on immunity and the immune system. They help counter immune depletion, and they improve the body's defenses by increasing the production of specialized immune cells, including helper T cells, B cells, NK cells, and regulatory T cells (Treg cells). Treg cells help maintain a tolerogenic state, preventing autoimmune disease. Adaptogens also have a direct effect on the nervous system, reducing stress-induced immune dysregulation.

Immune function is influenced by many factors, including stress, age, sleep (or lack thereof), gender, lifestyle, and nutritional status. Because adaptogens provide a nonspecific defense response to stress, they also offer an increased resistance to pathogens and infection by providing increased immunity.

Most adaptogens have either immune amphoteric or immunostimulating properties. An immune amphoteric nourishes and strengthens the immune system, helping it regain its normal self-regulatory activity. Immune amphoterics are useful for immune excess conditions (allergies), immune depletion (cancer, HIV/AIDS, CFIDS, chronic Lyme disease), or hypo/hyper conditions, which include most autoimmune disease. Adaptogens that are immune amphoterics include American ginseng, ashwagandha, Asian ginseng, cordyceps, guduchi, holy basil, jiaogulan, licorice, reishi, schisandra, and shilajit. There are also immune amphoterics that are not adaptogens such as astragalus and maitake.

Immunostimulants or immune tonics boost activity of the immune system but are not known to have the ability to normalize excessive immune response. Immune stimulants include codonopsis, eleuthero, jiaogulan, morinda, prince seng, rhaponticum, rhodiola, shatavari, and white bryony.

Hans Selye's General Adaptation Syndrome

There are several models to look at when we talk about the biological reaction to stress. The most popular model over time has been Hans Selye's general adaptation syndrome (sometimes referred to as biological stress syndrome). There is also the homeostasis/allostasis concept originated by Peter Sterling and Joseph Eyer and later expanded by Bruce McEwen. Both of these models will be discussed.

Modern research on stress began during the 1930s with work that was carried out by Canadian professor Hans Selye. Selye defined stress as "the nonspecific response of the body to any demand made upon it." What he meant by *nonspecific* was that the stress response can result from a variety of different kinds of stressors (see the list of types of stressors at the beginning of this chapter).

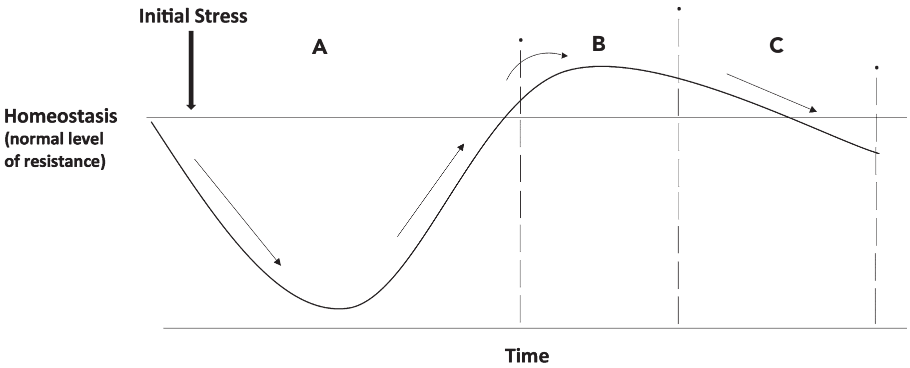
In 1936, Selye developed a theory called the general adaptation syndrome and hypothesized that stress is a major cause of disease because chronic stress causes long-term chemical changes within the body. He observed that given any source of external biological stress, the body responds with a predictable biological pattern in an attempt to restore its internal homeostasis. Selye also determined that there is a limited amount of adaptive energy and that this supply declines with continuous exposure to stressors.

Selye proposed that a human's adaptive response to stress had three stages: *alarm, resistance,* and *exhaustion*. Each stage can be defined by its underlying biochemical mechanisms.

Table 5.2. Hans Selye's General Adaptation Syndrome

STAGE	BIOCHEMICAL MECHANISM; METABOLIC ACTIVITY
Alarm	Defense response; HPA activation of adrenal glands and sympathetic nervous system, increased production of cortisol, epinephrine, and norepinephrine
Resistance	Adaptation to stress; increased production of cortisol in an attempt to resist stress
Exhaustion	Loss of ability to adapt due to the depletion of vital energy; damage to the organism

Table 5.3. Visual of the General Adaptation Syndrome



Legend:
A = alarm stage (onset of stress, decreased resistance to stress)
B = resistance stage (adaptation and increased resistance to stress, increased cortisol)
C = exhaustion stage (decompensation, HPA axis depletion)

Alarm Stage

When we are under stress, the body's first response is called the alarm reaction. This is the body's recognition of danger and its preparation to deal with threats. It is the immediate reaction to a stressor (physical, emotional, or environmental). The body responds by producing hormones for a fight-or-flight response and to mobilize energy.

At this stage, a person either reaches a point of optimal adaptation or suffers from too much stress. When the HPA axis is functioning properly, the body has adequate adaptive energy to deal with stress. When stress upsets the balance over time, the body transitions to the resistance stage.

Biology of the Alarm Stage

The initial alarm triggers the body's natural defense mechanism. The hypothalamus releases CRH and signals the pituitary glands to release ACTH, which affects the adrenal glands. This response is characterized as HPA axis activation. The adrenal glands release cortisol, adrenaline, and noradrenaline to increase the rate of metabolism, which in turn provides immediate energy. This acts to prepare the body for fight or flight. The adrenal glands also release DHEA.

The secretion of adrenaline and noradrenaline into the bloodstream produces several effects, including a narrowing of capillaries, an elevation of the blood pressure and heart rate, an increase of the blood sugar level, and a reduction of the functional activity of the digestive system.

The alarm reaction can be harmful to the body because it's actually an overreaction, resulting in the production of much more adrenaline than is necessary for coping with stress. If this overproduction is not used by physical activity, it can become harmful. With too much adrenaline, the resulting surges in blood pressure can damage the blood vessels of the heart and brain, increasing the risk of heart attack or stroke.

The body also produces excess cortisol, which causes catabolic processes that break down cells and destroy muscles. Many health problems and diseases are due to (or exacerbated by) elevated cortisol levels, including atherosclerosis, hypertension, stroke, gastric ulcers, metabolic syndrome, depression, polycystic ovary syndrome (PCOS), anxiety, and insomnia.

Alarm Stage: Adaptogen Response

Adaptogens build up adaptive energy and enhance overall vitality. They do this by normalizing the production of hormones produced by the body. They modulate cortisol levels. Adaptogens work in a natural way to restore hypothalamic sensitivity so that far less cortisol is required. One way they do this is by affecting the feedback control mechanism, making it more responsive so the hormonal feedback response is cut off faster.

In addition, adaptogens reduce stress reactions in the alarm phase, thereby delaying or avoiding the exhaustion stage. They recharge the adrenal glands, which are the body's mechanism for responding to stress and emotional changes. They also fine-tune and make the best use of resources to keep the body in balance and prepare the body to resume homeostasis after stressors are removed.

Resistance Stage

In this stage, the body adapts to resist stress and attempts to deal with the stressors it is exposed to. If the stressors continue to be present, then resistance also continues. Hormone levels may return to normal, and the body may have reduced defenses (adaptive energy) left. If the body learns to cope efficiently with the stressors, the stress may be resolved and the body returns to its normal resting state. If not, exhaustion follows.

Biology of the Resistance Stage

This stage of resistance is marked by a continued state of arousal. If the stressful situation is prolonged, the high level of hormones may upset homeostasis and harm internal organs, leaving the body vulnerable to disease.

When healthy, we can usually handle some amount of resistance, unless we are wasting all of our energy coping with an overload of stress hormones in the body. Adaptive energy declines with increased exposure to stressors.

Resistance causes an increase in cortisol and a decrease in DHEA. Stress can also disrupt the regular circadian (time-related) secretion of cortisol.

Resistance Stage: Adaptogen Response

Adaptogens can fine-tune the stress response by increasing adaptive energy. They help the body adapt to stress by inducing a state of non-specific resistance. This helps the body defend itself against the adverse effects of stress, whether they are biological, physical, or environmental in nature. In addition, adaptogens upregulate heat shock proteins, which protect the mitochondria from stress-induced damage; FOXO (forkhead box type O transcription factor), which inhibits the physiological effects of stress; and neuropeptide Y (NPY), which reduces anxiety, lowers blood pressure, and inhibits addiction and cortisol release.

Exhaustion Stage

At this stage, the stress has continued for some time. This is the point at which the body loses its ability to adapt because its energy supply is depleted. The adaptation process is over and stress adversely affects the body. Exhaustion can lead to fatigue, immune system dysfunction, and other symptoms and diseases.

Biology of the Exhaustion Stage

This stage of exhaustion occurs as a result of chronic stress. The energy of adaptation is used up, and the resistance of the organism becomes overwhelmed. This state sometimes is called adrenal fatigue, maladaptation, or dysfunction.

Adrenal dysfunction can be caused by the following conditions: (1) an excess or inadequacy of cortisol, DHEA, ACTH, and/or CRH, (2) relative imbalances of these hormones and releasing factors, (3) a loss of sensitivity of the hypothalamus and pituitary gland to the normal inhibiting effects of these hormones, and (4) depletion of energy reserves and a general loss of adaptative ability.

Exhaustion Stage: Adaptogen Response

The theory behind using adaptogens to relieve or prevent stress holds that adaptogenic herbs will lessen the reactions of the alarm phase and thereby delay or minimize the onset of exhaustion. Research has shown that adaptogens can reverse the depletion of adrenal cortisol associated with adrenal dysfunction.

Homeostasis and Allostasis

Brekhman and Dardymov noted that adaptogens have a normalizing influence on a body's physiology. The normalized condition has been called homeostasis. Selye defined stress as a state of threatened homeostasis. So, what is homeostasis, a term that represents a fundamental paradigm in the study of physiology?

Homeostasis is often described as the body's need to maintain a steady internal state, a state of equilibrium or balance. It comes from the Greek root words *homeo,* meaning "same," and *stasis,* meaning "stable"—remaining stable by staying the same. Many bodily conditions must not only remain constant, they must stay the same or at least within fixed, prescribed limits.

Examples of bodily components that should operate in a state of homeostasis include temperature, blood pressure, fluid and electrolyte balance, and the amount of oxygen that reaches the brain. Each of these components is held to a precise value called the set point. Although these set points can change over time, from day to day they are remarkably fixed. If they change by much, a person can die.

The term *allostasis,* first introduced by scientists Peter Sterling and Joseph Eyer, describes an additional process of reestablishing homeostasis, one that responds to a challenge instead of a constant flux.

Rather than referring to all responses to biological situations as *stress,* two new terms were introduced: *allostasis* and *allostatic load*. *Allostasis* comes from the Greek root words *allo,* meaning "variable," and *stasis,* meaning "stable"—maintaining stability (homeostasis) through change. *Allostasis is simply the ability to achieve stability through change.*

Our lives are constantly changing, and the body responds to change by adapting and achieving stability—allostasis. Examples of allostasis variables include extreme heat, extreme cold, infection, physical trauma, and psychological and emotional threats.

For example, the homeostatic process can adjust internal body temperature in response to climate changes that come with the changing seasons. However, *allostasis* is the term used to describe the condition of the body (under stress) when it's exposed to unexpected events such as a sudden drop in temperature or prolonged severe temperatures.

In this case, the body must react, adapt, and regain homeostasis to survive.

Biology of Allostasis

There are many examples of the body adapting to achieve allostasis, which is stability through change. Physiological mediators such as adrenaline act upon various organs to produce effects that are adaptive in the short run but can be damaging if the mediators are not shut off when no longer needed.

The concept of *allostatic load* refers to the wear and tear that the body experiences due to repeated cycles of allostasis as well as the inefficient turning-on or shutting-off of the body's responses to stress. Allostatic load is the cumulative biological burden exacted on the body by continued allostasis in attempts to adapt to life's demands.

The HPA axis is the foundation of allostasis and of allostatic load. It is where the nervous system and endocrine glands are brought together and held in balance—or not. The HPA axis is responsible for the adjustment phase of the allostatic response. Allostatic load can be measured, and cortisol levels serve as one of the indicators of HPA axis activity. Within the HPA axis, it is the function of the hypothalamus to maintain homeostasis and enhance allostasis.

Stress hormones (cortisol, adrenaline, noradrenaline, DHEA) are released as part of allostasis. Stress hormones, when over- or undersecreted, may tip the HPA axis out of balance. Over time, allostatic load can accumulate, and the overexposure to stress mediators can have adverse effects on various organ systems, leading to a state of allostatic overload in which serious changes can lead to disease. Allostatic overload can lead to a multitude of problems, including hypertension, obesity, diabetes, heart disease, depression, and asthma. It also can cause a decrease in immune system function, resulting in a reduction of NK-cell activity and a decline in immunoglobulin levels. Individuals differ in their health and well-being because they differ in the amounts of adaptive energy they have available. Protecting the body against overexposure to stress hormones is as important as the ability to mount an adequate allostatic response in the first place. Any type of imbalance in allostasis qualifies under the definition of the term *allostatic load*.

Adaptogens, Homeostasis, and Allostasis

Homeostasis and allostasis work together to regulate the human response to stress, and adaptogens help maintain homeostasis and prevent allostatic overload. Adaptogens assist the body in its ability to normalize homeostasis and enhance and improve allostasis. When regulated appropriately, the various stress hormones and stress mediators protect the body from a wide variety of stressors.

Adaptogens enable the body to maintain homeostasis for longer periods of time. Even if under stress, one can still perform effectively because homeostasis is not disrupted. Adaptogens also increase resistance to stress and prevent exhaustion.

State of Nonspecific Resistance

According to Lazarev and other Soviet scientists, adaptogens induce a state of nonspecific resistance in the body. This is a state of increased or heightened resistance that improves the body's response to stress. Adaptogens improve the capacity and sustaining power of the body to adapt to stress (adaptive response) and minimize the effects of stress.

Under stressful conditions, the body goes from its normal steady state of homeostasis to a heightened state of resistance. This heightened state of resistance stimulates nervous system, endocrine, and immune function in the short term (over time all of these systems become weakened by chronic stress).

As we have seen, adaptogens assist the body by both protecting against and reducing the effects of physiological or psychological stress. The following chapter continues the discussion of stress management and how adaptogens affect all areas of our health.