

● Homeostasis, Stress, and Adaptation

LEARNING OBJECTIVES ●

On completion of the chapter, the learner will be able to:

1. Relate the principles of internal constancy, homeostasis, stress, and adaptation to the concept of steady state.
2. Identify the significance of the body's compensatory mechanisms in promoting adaptation and maintaining the steady state.
3. Identify physiologic and psychosocial stressors.
4. Compare the sympathetic-adrenal-medullary response to stress to the hypothalamic-pituitary response to stress.
5. Describe the general adaptation syndrome as a theory of adaptation to biologic stress.
6. Describe the relationship of the process of negative feedback to the maintenance of the steady state.
7. Compare the adaptive processes of hypertrophy, atrophy, hyperplasia, dysplasia, and metaplasia.
8. Describe the inflammatory and reparative processes.
9. Assess the health patterns of an individual and determine their effects on maintenance of the steady state.
10. Identify ways in which maladaptive responses to stress can increase the risk of illness and cause disease.
11. Identify measures that are useful in reducing stress.
12. Specify the functions of social networks and support groups in reducing stress.

When the body is threatened or suffers an injury, its response may involve functional and structural changes; these changes may be adaptive (having a positive effect) or maladaptive (having a negative effect). The defense mechanisms that the body exhibits determine the difference between adaptation and maladaptation—health and disease.

Stress and Function

Physiology is the study of the functional activities of the living organism and its parts. Pathophysiology is the study of disordered function of the body. Each different body system performs specific functions to sustain optimal life for the organism. Mechanisms for adjusting internal conditions promote the normal steady state of the organism and ultimately its survival. These mechanisms are compensatory in nature and work to restore balance in the body. An example of this restorative effort is the development of rapid breathing (hyperpnea) after intense exercise in an attempt to compensate for an oxygen deficit and excess lactic acid accumulated in the muscle tissue.

Pathophysiologic processes result when cellular injury occurs at such a rapid rate that the body's compensatory mechanisms can no longer make the adaptive changes necessary to remain healthy. An example of a pathophysiologic change is the development of heart failure: the body reacts by retaining sodium and water and increasing venous pressure, which worsens the condition. These pathophysiologic mechanisms give rise to signs that are observed by the patient, nurse, or other health care provider, or symptoms that are reported by the patient. These observations, plus a sound knowledge of physiologic and pathophysiologic processes, can assist in determining the existence of a problem and can guide the nurse in planning the appropriate course of action.

Dynamic Balance: The Steady State

Physiologic mechanisms must be understood in the context of the body as a whole. The person, as a living system, has both an internal and an external environment, between which information

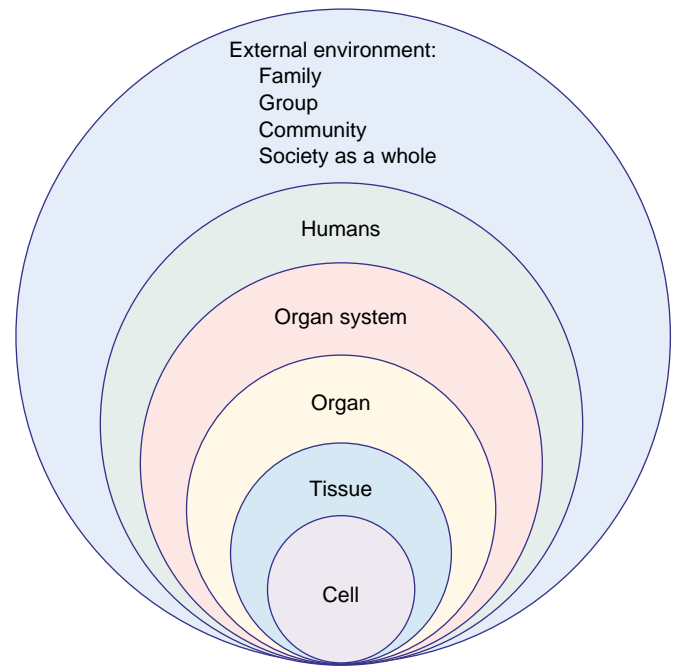


FIGURE 6-1 Constellation of systems. Each system is a subsystem of the larger system (suprasystem) of which it is a part. In this figure the cell is the smallest system, being a subsystem of all other systems.

and matter are continuously exchanged. Within the internal environment each organ, tissue, and cell is also a system or subsystem of the whole, each with its own internal and external environment, each exchanging information and matter (Fig. 6-1). The goal of the interaction of the body's subsystems is to produce a dynamic balance or **steady state** (even in the presence of change), so that all subsystems are in harmony with each other. Four concepts—constancy, homeostasis, stress, and adaptation—enhance the nurse's understanding of steady state.

Glossary

adaptation: a change or alteration designed to assist in adapting to a new situation or environment

adrenocorticotrophic hormone (ACTH): a hormone produced by the anterior lobe of the pituitary gland that stimulates the secretion of cortisone and other hormones by the adrenal cortex

antidiuretic hormone (ADH): a hormone secreted by the posterior lobe of the pituitary gland that constricts blood vessels, elevates blood pressure, and reduces the excretion of urine

catecholamines: any of the group of amines (such as epinephrine, norepinephrine, or dopamine) that serve as neurotransmitters

coping: the cognitive and behavioral strategies used to manage the stressors that tax a person's resources

dysplasia: a change in the appearance of a cell after exposure to chronic irritation

glucocorticoids: the group of steroid hormones, such as cortisol, that are produced

by the adrenal cortex; they are involved in carbohydrate, protein, and fat metabolism and have anti-inflammatory properties

gluconeogenesis: the formation of glucose, especially by the liver from noncarbohydrate sources such as amino acids and the glycerol portion of fats

guided imagery: use of the imagination to achieve relaxation or direct attention away from uncomfortable sensations or situations

homeostasis: a steady state within the body; the stability of the internal environment

hyperplasia: an increase in the number of new cells

hypoxia: inadequate supply of oxygen to the cell

infectious agents: biologic agents, such as viruses, bacteria, rickettsiae, mycoplasmas, fungi, protozoa, and nematodes, that cause disease in people

inflammation: a localized, protective reaction of tissue to injury, irritation, or infec-

tion, manifested by pain, redness, heat, swelling, and sometimes loss of function

metabolic rate: the speed at which some substances are broken down to yield energy for bodily processes and other substances are synthesized

metaplasia: a cell transformation in which a highly specialized cell changes to a less specialized cell

negative feedback: feedback that decreases the output of a system

positive feedback: feedback that increases the output of a system

steady state: a stable condition that does not change over time, or when change in one direction is balanced by change in an opposite direction

stress: a disruptive condition that occurs in response to adverse influences from the internal or external environments

vasoconstriction: the narrowing of a blood vessel

HISTORICAL THEORIES OF THE STEADY STATE

Claude Bernard, a 19th-century French physiologist, developed the biologic principle that for life there must be a constancy or “fixity of the internal milieu” despite changes in the external environment. The internal milieu was the fluid that bathed the cells, and the constancy was the balanced internal state maintained by physiologic and biochemical processes. His principle implied a static process.

Later, Walter Cannon used the term *homeostasis* to describe the stability of the internal environment, which, he said, was coordinated by homeostatic or compensatory processes that responded to changes in the internal environment. Any change within the internal environment initiated a “righting” response to minimize the change. These biologic processes sought physiologic and chemical balance and were under involuntary control.

Rene Jules Dubos (1965) provided further insight into the dynamic nature of the internal environment with his theory that two complementary concepts, homeostasis and adaptation, were necessary for balance. Homeostatic processes occurred quickly in response to stress, rapidly making the adjustments necessary to maintain the internal environment. Adaptive processes resulted in structural or functional changes over time. Dubos also emphasized that acceptable ranges of response to stimuli existed and that these responses varied for different individuals: “Absolute constancy is only a concept of the ideal.” Homeostasis and adaptation were both necessary for survival in a changing world.

Homeostasis, then, refers to a steady state within the body. When a change or stress occurs that causes a body function to deviate from its stable range, processes are initiated to restore and maintain the dynamic balance. When these adjustment processes or compensatory mechanisms are not adequate, the steady state is threatened, function becomes disordered, and pathophysiologic mechanisms occur. The pathophysiologic processes can lead to disease and may be active during disease, which is a threat to the steady state. Disease is an abnormal variation in the structure or function of any part of the body. It disrupts function and therefore limits the person’s freedom of action.

STRESS AND ADAPTATION

Stress is a state produced by a change in the environment that is perceived as challenging, threatening, or damaging to the person’s dynamic balance or equilibrium. The person is, or feels, unable to meet the demands of the new situation. The change or stimulus that evokes this state is the stressor. The nature of the stressor is variable; an event or change that will produce stress in one person may be neutral for another, and an event that produces stress at one time and place for one person may not do so for the same person at another time and place. A person appraises and copes with changing situations. The desired goal is **adaptation**, or adjustment to the change so that the person is again in equilibrium and has the energy and ability to meet new demands. This is the process of **coping** with the stress, a compensatory process with physiologic and psychological components.

Adaptation is a constant, ongoing process that requires a change in structure, function, or behavior so that the person is better suited to the environment; it involves an interaction between the person and the environment. The outcome depends on the degree of “fit” between the skills and capacities of the person, the type of social support available, and the various challenges or stressors being confronted. As such, adaptation is an individual

process: each individual has varying abilities to cope or respond. As new challenges are met, this ability to cope and adapt can change, thereby providing the individual with a wide range of adaptive ability. Adaptation occurs throughout the life span as the individual encounters many developmental and situational challenges, especially related to health and illness. The goal of these encounters is to promote adaptation. In situations of health and illness, this goal is realized by optimal wellness.

Because both stress and adaptation may exist at different levels of a system, it is possible to study these reactions at the cellular, tissue, and organ levels. Biologists are concerned mainly with subcellular components or with subsystems of the total body. Behavioral scientists, including many nurse researchers, study stress and adaptation in individuals, families, groups, and societies; they focus on how a group’s organizational features are modified to meet the requirements of the social and physical environment in which they exist. Adaptation is a continuous process of seeking harmony in an environment. The desired goals of adaptation for any system are survival, growth, and reproduction.

Stressors: Threats to the Steady State

Each person operates at a certain level of adaptation and regularly encounters a certain amount of change. Such change is expected; it contributes to growth and enhances life. Stressors, however, can upset this equilibrium. A stressor may be defined as an internal or external event or situation that creates the potential for physiologic, emotional, cognitive, or behavioral changes in an individual.

TYPES OF STRESSORS

Stressors exist in many forms and categories. They may be described as physical, physiologic, or psychosocial. Physical stressors include cold, heat, and chemical agents; physiologic stressors include pain and fatigue. Examples of psychosocial stressors are fear of failing an examination and losing a job. Stressors can also occur as normal life transitions that require some adjustment, such as going from childhood into puberty, getting married, or giving birth.

Stressors have also been classified as: (1) day-to-day frustrations or hassles; (2) major complex occurrences involving large groups, even entire nations; and (3) stressors that occur less frequently and involve fewer people. The first group, the day-to-day stressors, includes such common occurrences as getting caught in a traffic jam, experiencing computer downtime, and having an argument with a spouse or roommate. These experiences vary in effect; for example, encountering a rainstorm while one is vacationing at the beach will most likely evoke a more negative response than it might at another time. These less dramatic, frustrating, and irritating events—daily hassles—have been shown to have a greater health impact than major life events because of the cumulative effect they have over time. They can lead to high blood pressure, palpitations, or other physiologic problems (Jalowiec, 1993).

The second group of stressors influences larger groups of people, possibly even entire nations. These include events of history, such as terrorism and war, which are threatening situations when experienced either directly, in the war zone, or indirectly, as through live news coverage. The demographic, economic, and technological changes occurring in society also serve as stressors. The tension produced by any stressor is sometimes a result not only of the change itself, but also of the speed with which the change occurs.

The third group of stressors has been studied most extensively and concerns relatively infrequent situations that directly affect the individual. This category includes the influence of life events such as death, birth, marriage, divorce, and retirement. It also includes the psychosocial crises described by Erikson as occurring in the life cycle stages of the human experience. More enduring chronic stressors have also been placed in this category and may include such things as having a permanent functional disability or coping with the difficulties of providing long-term care to a frail elderly parent.

A stressor can also be categorized according to duration. It may be

- An acute, time-limited stressor, such as studying for final examinations
- A stressor sequence—a series of stressful events that result from an initial event such as job loss or divorce
- A chronic intermittent stressor, such as daily hassles
- A chronic enduring stressor that persists over time, such as chronic illness, a disability, or poverty

STRESS AS A STIMULUS FOR DISEASE

Relating life events to illness (the theoretical approach that defines stress as a stimulus) has been a major focus of psychosocial studies. This can be traced to Adolph Meyer, who in the 1930s observed in “life charts” of his patients a linkage between illnesses and critical life events. Subsequent research revealed that people under constant stress have a high incidence of psychosomatic disease.

Holmes and Rahe (1967) developed life events scales that assign numerical values, called life-change units, to typical life events. Because the items in the scales reflect events that require a change in a person’s life pattern, and stress is defined as an accumulation of changes in one’s life that require psychological adaptation, one can theoretically predict the likelihood of illness by checking off the number of recent events and deriving a total score. The Recent Life Changes Questionnaire (Tausig, 1982) contains 118 items such as death, birth, marriage, divorce, promotions, serious arguments, and vacations. The events listed include both desirable and undesirable circumstances.

Sources of stress for patients have been well researched (Baldard, 1981; Bryla, 1996; Jalowiec, 1993). People typically experience distress related to alterations in their physical and emotional health status, changes in their level of daily functioning, and decreased social support or the loss of significant others. Fears of immobilization, isolation, loneliness, sensory changes, financial problems, and death or disability increase a person’s anxiety level. Loss of one’s role or perceived purpose in life can cause intense discomfort. Any of these identified variables plus a myriad of other conditions or overwhelming demands are likely to cause ineffective coping, and a lack of necessary coping skills is often a source of additional distress for an individual. When a person endures prolonged or unrelenting suffering, the outcome is frequently the development of a stress-related illness. Nurses possess the skills to assist people to alter their distressing circumstances and manage their responses to stress.

PSYCHOLOGICAL RESPONSES TO STRESS

After the recognition of a stressor, an individual consciously or unconsciously reacts to manage the situation. This is called the mediating process. A theory developed by Lazarus (1991a) emphasizes

cognitive appraisal and coping as important mediators of stress. Appraisal and coping are influenced by antecedent variables that include the internal and external resources of the person.

Appraisal of the Stressful Event

Cognitive appraisal (Lazarus, 1991a; Lazarus & Folkman, 1984) is a process by which an event is evaluated with respect to what is at stake (primary appraisal) and what might and can be done (secondary appraisal). What individuals see as being at stake is influenced by their personal goals, commitments, or motivations. Important factors include how important or relevant the event is to them, whether the event conflicts with what they want or desire, and whether the situation threatens their own sense of strength and ego identity.

As an outcome of primary appraisal, the situation is identified as either nonstressful or stressful. If nonstressful, the situation is irrelevant or benign (positive). A stressful situation may be one of three kinds: (1) one in which harm or loss has occurred; (2) one that is threatening, in that harm or loss is anticipated; and (3) one that is challenging, in that some opportunity or gain is anticipated.

Secondary appraisal is an evaluation of what might and can be done about this situation. Actions include assigning blame to those responsible for a frustrating event, thinking about whether one can do something about the situation (coping potential), and determining future expectancy, or whether things are likely to change for better or worse (Lazarus, 1991a, 1991c). A comparison of what is at stake and what can be done about it (a type of risk–benefit analysis) determines the degree of stress.

Reappraisal, a change of opinion based on new information, also occurs. The appraisal process is not necessarily sequential; primary and secondary appraisal and reappraisal may occur simultaneously. Information learned from an adaptational encounter can be stored, so that when a similar situation is encountered again the whole process does not need to be repeated.

The appraisal process contributes to the development of an emotion. Negative emotions such as fear and anger accompany harm/loss appraisals, and positive emotions accompany challenge. In addition to the subjective component or feeling that accompanies a particular emotion, each emotion also includes a tendency to act in a certain way. For example, an unexpected quiz in the classroom might be judged as threatening by unprepared students. They might feel fear, anger, and resentment and might express these emotions outwardly with hostile behavior or comments.

Lazarus (1991a) expanded his former ideas about stress, appraisal, and coping into a more complex model relating emotion to adaptation. He called this model a “cognitive-motivational-relational theory,” with the term *relational* “standing for a focus on negotiation with a physical and social world” (p. 13). A theory of emotion was proposed as the bridge to connect psychology, physiology, and sociology: “More than any other arena of psychological thought, emotion is an integrative, organismic concept that subsumes psychological stress and coping within itself and unites motivation, cognition, and adaptation in a complex configuration” (p. 40).

Coping With the Stressful Event

Coping, according to Lazarus, consists of the cognitive and behavioral efforts made to manage the specific external or internal demands that tax a person’s resources and may be emotion-focused or problem-focused. Coping that is emotion focused seeks to make the person feel better by lessening the emotional distress

felt. Problem-focused coping aims to make direct changes in the environment so that the situation can be managed more effectively. Both types of coping usually occur in a stressful situation. Even if the situation is viewed as challenging or beneficial, coping efforts may be required to develop and sustain the challenge—that is, to maintain the positive benefits of the challenge and to ward off any threats. In harmful or threatening situations, successful coping reduces or eliminates the source of stress and relieves the emotion it generated.

Appraisal and coping are affected by internal characteristics such as health, energy, personal belief systems, commitments or life goals, self-esteem, control, mastery, knowledge, problem-solving skills, and social skills. The characteristics that have been studied most often in nursing research are health-promoting lifestyles and hardiness. A health-promoting lifestyle buffers the effect of stressors. From a nursing practice standpoint, this outcome—buffering the effect of stressors—supports nursing’s goal of promoting health. In many circumstances, promoting a healthy lifestyle is more achievable than altering the stressors.

Hardiness is the name given to a general quality that comes from having rich, varied, and rewarding experiences. It is a personality characteristic composed of control, commitment, and challenge. Hardy people perceive stressors as something they can change and therefore control. To them, potentially stressful situations are interesting and meaningful; change and new situations are viewed as challenging opportunities for growth. Some positive support has been found for hardiness as a significant variable that positively influences rehabilitation and overall improvement after an onset of an acute or chronic illness (Felton, 2000; Williams, 2000).

PHYSIOLOGIC RESPONSE TO STRESS

The physiologic response to a stressor, whether it is a physical stressor or a psychological stressor, is a protective and adaptive mechanism to maintain the homeostatic balance of the body. The stress response is a “cascade of neural and hormonal events that have short- and long-lasting consequences for both brain and body . . . ; a stressor is an event that challenges homeostasis, with a disease outcome being looked upon as a failure of the normal process of adaptation to the stress” (McEwen & Mendelson, 1993, p. 101).

The General Adaptation Syndrome

Hans Selye developed a theory of adaptation that profoundly influenced the scientific study of stress. In 1936, Selye, experimenting with animals, first described a syndrome consisting of enlargement of the adrenal cortex; shrinkage of the thymus, spleen, lymph nodes, and other lymphatic structures; and the appearance of deep, bleeding ulcers in the stomach and duodenum. He identified this as a nonspecific response to diverse, noxious stimuli. From this beginning, he developed a theory of adaptation to biologic stress that he named the general adaptation syndrome.

PHASES OF THE GENERAL ADAPTATION SYNDROME

The general adaptation syndrome has three phases: alarm, resistance, and exhaustion. During the alarm phase, the sympathetic “fight-or-flight” response is activated with release of **catecholamines** and the onset of the **adrenocorticotropic hormone (ACTH)**—adrenal cortical response. The alarm reaction is defensive and anti-inflammatory but self-limited. Because living in a continuous state of alarm would result in death, the person moves

into the second stage, resistance. During this stage, adaptation to the noxious stressor occurs, and cortisol activity is still increased. If exposure to the stressor is prolonged, exhaustion sets in and endocrine activity increases. This produces deleterious effects on the body systems (especially the circulatory, digestive, and immune systems) that can lead to death. Stages one and two of this syndrome are repeated, in different degrees, throughout life as the person encounters stressors.

Selye compared the general adaptation syndrome with the life process. During childhood, there are too few encounters with stress to promote the development of adaptive functioning, and the child is vulnerable. During adulthood, the person encounters a number of life’s stressful events and develops a resistance or adaptation. During the later years, the accumulation of life’s stressors and the wear and tear on the organism again deplete the person’s ability to adapt, resistance falls, and eventually death occurs.

LOCAL ADAPTATION SYNDROME

According to Selye’s theory, a local adaptation syndrome also occurs. This syndrome includes the inflammatory response and repair processes that occur at the local site of tissue injury. The local adaptation syndrome occurs in small, topical injuries, such as contact dermatitis. If the local injury is severe enough, the general adaptation syndrome is activated as well.

Selye emphasized that stress is the nonspecific response common to all stressors, regardless of whether they are physiologic, psychological, or social. The many conditioning factors in each person’s environment account for why different demands are interpreted by different people as stressors. Conditioning factors also account for differences in the tolerance of different people for stress: some people may develop diseases of adaptation, such as hypertension and migraine headaches, while others are unaffected.

Interpretation of Stressful Stimuli by the Brain

Physiologic responses to stress are mediated by the brain through a complex network of chemical and electrical messages. The neural and hormonal actions that maintain homeostatic balance are integrated by the hypothalamus, which is located in the center of the brain, surrounded by the limbic system and the cerebral hemispheres. The hypothalamus integrates autonomic nervous system mechanisms that maintain the chemical constancy of the internal environment of the body. Together with the limbic system, it also regulates emotions and many visceral behaviors necessary for survival (eg, eating, drinking, temperature control, reproduction, defense, aggression). The hypothalamus is made up of a number of nuclei; the limbic system contains the amygdala, hippocampus, and septal nuclei, along with other structures.

Literature supports the concept that each of these structures responds differently to stimuli, and each has its own characteristic response (Watkins, 1997). The cerebral hemispheres are concerned with cognitive functions: thought processes, learning, and memory. The limbic system has connections with both the cerebral hemispheres and the brain stem. In addition, the reticular activating system, which is a network of cells that forms a two-way communication system, extends from the brain stem into the midbrain and limbic system. This network controls the alert or waking state of the body.

In the stress response, afferent impulses are carried from sensory organs (eye, ear, nose, skin) and internal sensors (baroreceptors, chemoreceptors) to nerve centers in the brain. The response to the perception of stress is integrated in the hypothalamus,

which coordinates the adjustments necessary to return to homeostatic balance. The degree and duration of the response varies; major stress evokes both sympathetic and pituitary adrenal responses.

Neural and neuroendocrine pathways under the control of the hypothalamus are also activated in the stress response. First, there is a sympathetic nervous system discharge, followed by a sympathetic-adrenal-medullary discharge. If the stress persists, the hypothalamic-pituitary system is activated (Fig. 6-2).

SYMPATHETIC NERVOUS SYSTEM RESPONSE

The sympathetic nervous system response is rapid and short-lived. Norepinephrine is released at nerve endings that are in direct contact with their respective end organs to cause an increase in function of the vital organs and a state of general body arousal. The heart rate is increased and peripheral **vasoconstriction** occurs, raising the blood pressure. Blood is also shunted away from abdominal organs. The purpose of these activities is to provide better perfusion of vital organs (brain, heart, skeletal muscles).

Blood glucose is increased, supplying more readily available energy. The pupils are dilated, and mental activity is increased; a greater sense of awareness exists. Constriction of the blood vessels of the skin limits bleeding in the event of trauma. The person is likely to experience cold feet, clammy skin and hands, chills, palpitations, and a knot in the stomach. Typically, the person appears tense, with the muscles of the neck, upper back, and shoulders tightened; respirations may be rapid and shallow, with the diaphragm tense.

SYMPATHETIC-ADRENAL-MEDULLARY RESPONSE

In addition to its direct effect on major end organs, the sympathetic nervous system also stimulates the medulla of the adrenal gland to release the hormones epinephrine and norepinephrine into the bloodstream. The action of these hormones is similar to that of the sympathetic nervous system and have the effect of sustaining and prolonging its actions. Epinephrine and norepinephrine are catecholamines that stimulate the nervous system and produce metabolic effects that increase the blood glucose level



Physiology/Pathophysiology

FIGURE 6-2 Integrated responses to stress mediated by the sympathetic nervous system and the hypothalamic–pituitary–adrenocortical axis. The responses are mutually reinforcing, at both the central and peripheral levels. Negative feedback by cortisol also can limit an overresponse that might be harmful to the individual. *Colored arrows*, stimulation; *open arrows*, inhibition; CRH, corticotropin-releasing hormone; ACTH, adrenocorticotropic hormone. Reproduced with permission from Berne, R. M., & Levy, M. N. (1993). *Physiology*. St. Louis: C. V. Mosby.

and increase the **metabolic rate**. The effect of the sympathetic and adrenal-medullary responses is summarized in Table 6-1. This effect is called the “fight-or-flight” reaction.

HYPOTHALAMIC-PITUITARY RESPONSE

The longest-acting phase of the physiologic response, which is more likely to occur in persistent stress, involves the hypothalamic-pituitary pathway. The hypothalamus secretes corticotropin-releasing factor, which stimulates the anterior pituitary to produce ACTH. ACTH in turn stimulates the adrenal cortex to produce **glucocorticoids**, primarily cortisol. Cortisol stimulates protein catabolism, releasing amino acids; stimulates liver uptake of amino acids and their conversion to glucose (**gluconeogenesis**); and inhibits glucose uptake (anti-insulin action) by many body cells but not those of the brain and heart. These cortisol-induced metabolic effects provide the body with a ready source of energy during a stressful situation. This effect has some important implications. For example, a person with diabetes who is under stress, such as that caused by an infection, needs more insulin than usual. Any patient who is under stress (caused, for example, by illness, surgery, trauma or prolonged psychological stress) catabolizes body protein and needs supplements. Children subjected to severe stress have retarded growth.

The actions of the catecholamines (epinephrine and norepinephrine) and cortisol are the most important in the general response to stress. Other hormones released are **antidiuretic hormone (ADH)** from the posterior pituitary and aldosterone from the adrenal cortex. ADH and aldosterone promote sodium and water retention, which is an adaptive mechanism in the event of hemorrhage or loss of fluids through excessive perspiration. ADH has also been shown to influence learning and may thus facilitate coping in new and threatening situations. Secretion of growth hormone and glucagon stimulates the uptake of amino acids by

cells, helping to mobilize energy resources. Endorphins, which are endogenous opiates, increase during stress and enhance the threshold for tolerance of painful stimuli. They may also affect mood and have been implicated in the so-called “high” that long-distance runners experience. The secretion of other hormones is also affected, but their adaptive function is less clear.

IMMUNOLOGIC RESPONSE

Research findings show that the immune system is connected to the neuroendocrine and autonomic systems. Lymphoid tissue is richly supplied by autonomic nerves capable of releasing a number of different neuropeptides that can have a direct effect on leukocyte regulation and the inflammatory response. Neuroendocrine hormones released by the central nervous system and endocrine tissues can inhibit or stimulate leukocyte function. The wide variety of stressors people experience may result in different alterations in autonomic activity and subtle variations in neurohormone and neuropeptide synthesis. All of these possible autonomic and neuroendocrine responses can interact to initiate, weaken, enhance, or terminate an immune response (Watkins, 1997).

The study of the relationships among the neuroendocrine system, the central and autonomic nervous systems, and the immune system and the effects of these relationships on overall health outcomes is called *psychoneuroimmunology*. Because one’s perception of events and coping styles determine whether, and to what extent, an event activates the stress response system, and because the stress response affects immune activity, one’s perceptions, ideas, and thoughts can have profound neurochemical and immunologic consequences. Multiple studies have demonstrated alteration of immune function in people who are under stress, as evidenced by a decrease in the number of leukocytes, impaired immune response to immunizations, and diminished cytotoxic-

Table 6-1 • Sympathetic–Adrenal–Medullary Response to Stress

EFFECT	PURPOSE	MECHANISM
Increased heart rate and blood pressure	Better perfusion of vital organs	Increased cardiac output due to increased myocardial contractility and heart rate; increased venous return (peripheral vasoconstriction)
Increased blood glucose level	Increased available energy	Increased liver and muscle glycogen breakdown; increased breakdown of adipose tissue triglycerides
Mental acuity	Alert state	Increase in amount of blood shunted to the brain from the abdominal viscera and skin
Dilated pupils	Increased awareness	Contraction of radial muscle of iris
Increased tension of skeletal muscles	Preparedness for activity, decreased fatigue	Excitation of muscles; increase in amount of blood shunted to the muscles from the abdominal viscera and skin
Increased ventilation (may be rapid and shallow)	Provision of oxygen for energy	Stimulation of respiratory center in medulla; bronchodilation
Increased coagulability of blood	Prevention of hemorrhage in event of trauma	Vasoconstriction of surface vessels

ity of natural killer cells (Andersen et al., 1998; Constantino, Secula, Rabin, & Stone, 2000; Glaser & Kiecolt-Glaser, 1997; Pike et al., 1997; Robinson, Matthews, & Witek-Janusek, 2000). Other studies have identified certain personality traits, such as optimism and active coping, as having positive effects on health or specific immune measures (Chalfont & Bennett, 1999; Goodkin et al., 1996; Kennedy, 2000; Sergerstrom, Fahey, Kemeny, & Taylor, 1998). As research continues, this new field of study will continue to uncover to what extent and by what mechanisms people can consciously influence their immunity.

MALADAPTIVE RESPONSES TO STRESS

The stress response, which, as indicated earlier facilitates adaptation to threatening situations, has been retained from our evolutionary past. The “fight-or-flight” response, for example, is an anticipatory response that mobilized the bodily resources of our ancestors to deal with predators and other harsh factors in their environment. This same mobilization comes into play in response to emotional stimuli unrelated to danger. For example, a person may get an “adrenaline rush” when competing over a decisive point in a ball game, or when excited about attending a party.

When the responses to stress are ineffective, they are referred to as *maladaptive*. Maladaptive responses are chronic, recurrent responses or patterns of response over time that do not promote the goals of adaptation. The goals of adaptation are somatic or physical health (optimal wellness); psychological health or having a sense of well-being (happiness, satisfaction with life, morale); and enhanced social functioning, which includes work, social life, and family (positive relationships). Maladaptive responses that threaten these goals include faulty appraisals and inappropriate coping (Lazarus, 1991a).

The frequency, intensity, and duration of stressful situations contribute to the development of negative emotions and subsequent patterns of neurochemical discharge. By appraising situations more adequately and coping more appropriately, it is possible to anticipate and defuse some of these situations. For example, frequent potentially stressful encounters (eg, marital discord) might be avoided with better communication and problem solving, or a pattern of procrastination (eg, delaying work on tasks) could be corrected to reduce stress when deadlines approach.

Coping processes that include the use of alcohol or drugs to reduce stress increase the risk of illness. Other inappropriate coping patterns may increase the risk of illness less directly. For example, people who demonstrate “type A” personality behaviors such as impatience, competitiveness, and achievement orientation and have an underlying hostile approach to life are more prone than others to develop stress-related illnesses. Type A behaviors increase the output of catecholamines, the adrenal-medullary hormones, with their attendant effects on the body.

Other forms of inappropriate coping include denial, avoidance, and distancing. Denial may be illustrated by the woman who feels a lump in her breast but downplays its seriousness and delays seeking medical attention. The intent of denial is to control the threat, but it may also endanger life.

Models of illness frequently cite stress and maladaptation as precursors to disease. A general model of illness, based on Selye’s theory, suggests that any stressor elicits a state of disturbed physiologic equilibrium. If this state is prolonged or the response is excessive, it will increase the susceptibility of the person to illness. This susceptibility, coupled with a predisposition in the person

(whether from genetic traits, health, or age), leads to illness. If the sympathetic adrenal-medullary response is prolonged or excessive, a state of chronic arousal develops that may lead to high blood pressure, arteriosclerotic changes, and cardiovascular disease. If the production of the ACTH is prolonged or excessive, behavior patterns of withdrawal and depression are seen. In addition, the immune response is decreased, and infections and tumors may develop.

Selye (1976) proposed a list of disorders that he called diseases of maladaptation: high blood pressure, diseases of the heart and blood vessels, diseases of the kidney, hypertension of pregnancy, rheumatic and rheumatoid arthritis, inflammatory diseases of the skin and eyes, infections, allergic and hypersensitivity diseases, nervous and mental diseases, sexual derangements, digestive diseases, metabolic diseases, and cancer.

INDICATORS OF STRESS

Indicators of stress and the stress response include both subjective and objective measures. Chart 6-1 lists signs and symptoms that may be observed directly or reported by the person. They are psychological, physiologic, or behavioral and reflect social behaviors and thought processes. Some of these reactions may be coping behaviors. Over time, each person tends to develop a characteristic pattern of behavior during stress that is a warning that the system is out of balance.

Laboratory measurements of indicators of stress have helped in understanding this complex process. Among the measures, blood and urine analyses can be used to demonstrate changes in hormonal levels and hormonal breakdown products. Reliable measures of stress include blood levels of catecholamines, corticoids, ACTH, and eosinophils. The serum creatine/creatinine ratio and elevations of cholesterol and free fatty acids can also be measured. Immunoglobulin assays may be determined. With greater attention to neuroimmunology, improved laboratory measures are likely to follow. Increases in blood pressure and heart rate can also be measured.

In addition to using laboratory tests, researchers have developed questionnaires to identify and assess stressors, stress, and coping strategies. Many of these are discussed in the research monograph developed by Barnfather and Lyon (1993), which was based on a synthesis conference held by nurse scientists on the state of the science in stress and coping nursing research. Some examples of the research instruments that nurses commonly use to measure levels of client distress and client functioning can be found in a variety of research reports (Cronquist, Wredning, Norlander, Langius, & Bjorvell, 2000; Starzonski & Hilton, 2000). Miller and Smith (1993) provided a stress audit and a stress profile measurement tool that is available in the popular lay literature.

NURSING IMPLICATIONS

It is important for the nurse to realize that the optimal point of intervention to promote health is during the stage when the individual's own compensatory processes are still functioning. Early identification of both physiologic and psychological stressors remains a major role of the nurse, and information on the interrelationships between physical and emotional health can be found in research journals. The nurse should be able to relate the presenting signs and symptoms of distress to the physiology they represent and identify the individual's position on the continuum of function, from health and compensation to pathophysiology and disease. For example, if an anxious middle-aged woman presented for a checkup and was found to be overweight, with a blood pressure of 130/85 mm Hg, the nurse would counsel her with respect to diet, stress management, and activity. The nurse would also encourage weight loss and discuss the woman's intake of salt (which affects fluid balance) and caffeine (which provides a stimulant effect). The patient and the nurse would identify both individual and environmental stressors and discuss strategies to decrease the lifestyle stress, with the ultimate goal being to create a healthy lifestyle and prevent hypertension and its sequelae.

Stress at the Cellular Level

Pathologic processes may occur at all levels of the biologic organism. If the cell is considered the smallest unit or subsystem (tissues being aggregates of cells, organs aggregates of tissues, and so forth), the processes of health and disease or adaptation and maladaptation can all occur at the cellular level. Indeed, pathologic processes are often described by scientists at the subcellular or molecular level.

The cell exists on a continuum of function and structure, ranging from the normal cell, to the adapted cell, to the injured or diseased cell, to the dead cell (Fig. 6-3). Changes from one state to another may occur rapidly and may not be readily de-

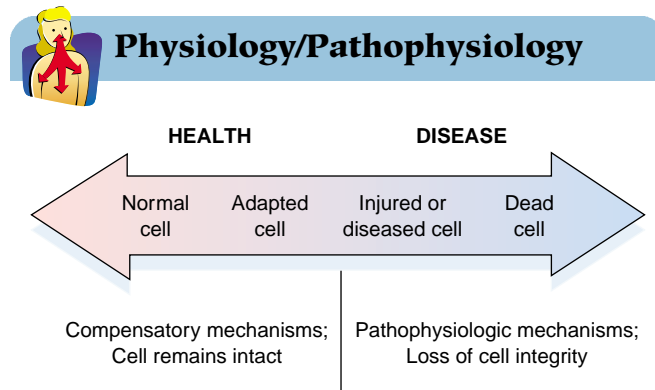


FIGURE 6-3 The cell on a continuum of function and structure. Changes in the cell are not as easily discerned as the diagram depicts. The point at which compensation subsides and pathophysiology begins is not clearly defined.

tectable, because each state does not have discrete boundaries, and disease represents an extension and distortion of normal processes. The earliest changes occur at the molecular or subcellular level and are not perceptible until steady-state functions or structures are altered. With cell injury, some changes may be reversible; in other instances, the injuries are lethal. For example, tanning of the skin is an adaptive, morphologic response to exposure to the rays of the sun. If the exposure is continued, however, sunburn and injury occur, and some cells may die, as evidenced by desquamation ("peeling").

Different cells and tissues respond to stimuli with different patterns and rates of response; some cells are more vulnerable to one type of stimulus or stressor than others. The cell involved, its ability to adapt, and its physiologic state are determinants of the response. For example, cardiac muscle cells respond to **hypoxia** (inadequate oxygenation) more quickly than smooth muscle cells do.

Other determinants of cellular response are the type or nature of the stimulus, its duration, and its severity. For example, neurons that control respiration can develop a tolerance to regular, small amounts of a barbiturate, but one large dose may result in respiratory depression and death.

CONTROL OF THE STEADY STATE

The concept of the cell as existing on a continuum of function and structure includes the relationship of the cell to compensatory mechanisms, which occur continuously in the body to maintain the steady state. Compensatory processes are regulated primarily by the autonomic nervous system and the endocrine system, with control achieved through negative feedback.

Negative Feedback

Negative feedback mechanisms throughout the body monitor the internal environment and restore homeostasis when conditions shift out of the normal range. These mechanisms work by sensing deviations from a predetermined set point or range of adaptability and triggering a response aimed at offsetting the deviation. Blood pressure, acid-base balance, blood glucose level, body temperature, and fluid and electrolyte balance are examples of functions regulated through such compensatory mechanisms.

Most of the human body's control systems are integrated by the brain and influenced by the nervous and endocrine systems. Control activities involve detecting deviations from the predetermined reference point and stimulating compensatory responses in the muscles and glands of the body. The major organs affected are the heart, lungs, kidneys, liver, gastrointestinal tract, and skin. When stimulated, these organs alter their rate of activity or the amount of secretions they produce. Because of this, they have been called the "organs of homeostasis or adjustment."

In addition to the responses controlled by the nervous and endocrine systems, local responses consisting of small feedback loops in a group of cells or tissues are possible. The cells detect a change in their immediate environment and initiate an action to counteract its effect. For example, the accumulation of lactic acid in an exercised muscle stimulates dilation of blood vessels in the area to increase blood flow and improve the delivery of oxygen and removal of waste products.

The net result of the activities of feedback loops is homeostasis. A steady state is achieved by the continuous, variable action of the organs involved in making the adjustments and by the continuous small exchanges of chemical substances among cells, interstitial fluid, and blood. For example, an increase in the carbon dioxide concentration of the extracellular fluid leads to increased pulmonary ventilation, which decreases the carbon dioxide level. On a cellular level, increased carbon dioxide raises the hydrogen ion concentration of the blood. This is detected by chemosensitive receptors in the respiratory control center of the medulla of the brain. The chemoreceptors stimulate an increase in the rate of discharge of the neurons that innervate the diaphragm and intercostal muscles, which increases the rate of respiration. Excess carbon dioxide is exhaled, the hydrogen ion concentration returns to normal, and the chemically sensitive neurons are no longer stimulated.

Positive Feedback

Another type of feedback, **positive feedback**, perpetuates the chain of events set in motion by the original disturbance instead of compensating for it. As the system becomes more unbalanced, disorder and disintegration occur. There are some exceptions to this; blood clotting in humans, for example, is an important positive feedback mechanism.

CELLULAR ADAPTATION

Cells are complex units that dynamically respond to the changing demands and stresses of daily life. They possess a maintenance function and a specialized function. The maintenance function refers to the activities that the cell must perform with respect to itself; specialized functions are those that the cell performs in relation to the tissues and organs of which it is a part. Individual cells may cease to function without posing a threat to the organism. As the number of dead cells increases, however, the specialized functions of the tissues are altered and the individual's health is threatened.

Cells can adapt to environmental stress through structural and functional changes. Some of these adaptations are hypertrophy, atrophy, hyperplasia, dysplasia, and metaplasia (Table 6-2).

Hypertrophy and atrophy lead to changes in the size of cells and hence the size of the organs they form. Compensatory hypertrophy is the result of an enlarged muscle mass and commonly occurs in skeletal and cardiac muscle that experiences a prolonged, increased workload. One example is the bulging muscles of the athlete who engages in body building.

Atrophy can be the consequence of a disease or of decreased use, decreased blood supply, loss of nerve supply, or inadequate nutrition. Disuse of a body part is often associated with the aging

Table 6-2 • Cellular Adaptation to Stressors

ADAPTATION	STIMULUS	EXAMPLE
Hypertrophy—increase in cell size leading to increase in organ size	Increased workload	Leg muscles of runner Arm muscles in tennis player Cardiac muscle in person with hypertension
Atrophy—shrinkage in size of cell, leading to decrease in organ size	Decrease in: Use Blood supply Nutrition Hormonal stimulation Innervation	Secondary sex organs in aging person Extremity immobilized in plaster cast
Hyperplasia—increase in number of new cells (increase in mitosis)	Hormonal influence	Breast changes of a girl in puberty or of a pregnant woman Regeneration of liver cells New red blood cells in blood loss
Dysplasia—change in the appearance of cells after they have been subjected to chronic irritation	Reproduction of cells with resulting alteration of their size and shape	Alterations in epithelial cells of the skin or the cervix, producing irregular tissue changes that could be the precursors of a malignancy
Metaplasia—transformation of one adult cell type to another (reversible)	Stress applied to highly specialized cell	Changes in epithelial cells lining bronchi in response to smoke irritation (cells become less specialized)

process. Cell size and organ size decrease; structures principally affected are the skeletal muscles, the secondary sex organs, the heart, and the brain.

Hyperplasia is an increase in the number of new cells in an organ or tissue. As cells multiply and are subjected to increased stimulation, the tissue mass enlarges. It is a mitotic response (a change occurring with mitosis), but it is reversible when the stimulus is removed. This distinguishes it from neoplasia or malignant growth, which continues after the stimulus is removed. Hyperplasia may be hormonally induced. An example is the increase in the size of the thyroid gland caused by thyroid-stimulating hormone (secreted from the pituitary gland) when a deficit in thyroid hormone is detected.

Dysplasia is the change in the appearance of cells after they have been subjected to chronic irritation. Dysplastic cells have a tendency to become malignant; dysplasia is seen commonly in epithelial cells in the bronchi of smokers.

Metaplasia is a cell transformation in which a highly specialized cell changes to a less specialized cell. This serves a protective function, because the less specialized cell is more resistant to the stress that stimulated the change. For example, the ciliated columnar epithelium lining the bronchi of smokers is replaced by squamous epithelium. The squamous cells can survive; loss of the cilia and protective mucus, however, can have damaging consequences.

These adaptations allow the survival of the organism. They also reflect changes in the normal cell in response to stress. If the stress is unrelenting, the function of the adapted cell may succumb, and cell injury will occur.

CELLULAR INJURY

Injury is defined as a disorder in steady-state regulation. Any stressor that alters the ability of the cell or system to maintain optimal balance of its adjustment processes will lead to injury. Structural and functional damage then occurs, which may be reversible (permitting recovery) or irreversible (leading to disability or death). Homeostatic adjustments are concerned with the small changes within the body's systems. With adaptive changes, compensation occurs and a steady state is achieved, although it may be at new levels. With injury, steady-state regulation is lost, and changes in functioning ensue.

Causes of disorder and injury in the system (cell, tissue, organ, body) may arise from the external or internal environment (Fig. 6-4) and include hypoxia, nutritional imbalance, physical agents, chemical agents, **infectious agents**, immune mechanisms, genetic defects, and psychogenic factors. The most common causes are hypoxia (oxygen deficiency), chemical injury, and infectious agents. In addition, the presence of one injury makes the system more susceptible to another injury. For example, inadequate oxygenation and nutritional deficiencies make the system vulnerable to infection. These agents act at the cellular level by damaging or destroying

- The integrity of the cell membrane, necessary for ionic balance
- The ability of the cell to transform energy (aerobic respiration, production of adenosine triphosphate)
- The ability of the cell to synthesize enzymes and other necessary proteins
- The ability of the cell to grow and reproduce (genetic integrity)

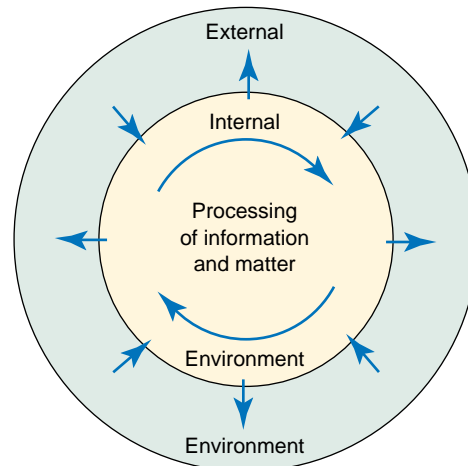


FIGURE 6-4 Influences leading to disorder may arise from the internal environment and the external environment of the system. Excesses or deficits of information and matter may occur, or there may be faulty regulation of processing.

Hypoxia

Inadequate cellular oxygenation (hypoxia) interferes with the cell's ability to transform energy. Hypoxia may be caused by:

- A decrease in blood supply to an area
- A decrease in the oxygen-carrying capacity of the blood (decreased hemoglobin)
- A ventilation/perfusion or respiratory problem that reduces the amount of oxygen available in the blood
- A problem in the cell's enzyme system that makes it unable to use the oxygen delivered to it

The usual cause is ischemia, or deficient blood supply. Ischemia is commonly seen in myocardial cell injury in which arterial blood flow is decreased because of atherosclerotic narrowing of blood vessels. Ischemia also results from intravascular clots (thrombi or emboli) that may form and interfere with blood supply. Thrombi and emboli are common causes of cerebrovascular accidents (strokes). The length of time different tissues can survive without oxygen varies. For example, brain cells may succumb in 3 to 6 minutes, depending on the situation. If the condition leading to hypoxia is slow and progressive, collateral circulation may develop, whereby blood is supplied by other blood vessels in the area. However, this mechanism is not highly reliable.

Nutritional Imbalance

Nutritional imbalance refers to a relative or absolute deficiency or excess of one or more essential nutrients. This may be manifested as undernutrition (inadequate consumption of food or calories) or overnutrition (caloric excess). Caloric excess to the point of obesity overloads cells in the body with lipids. By requiring more energy to maintain the extra tissue, obesity places a strain on the body and has been associated with the development of disease, especially pulmonary and cardiovascular disease.

Specific deficiencies arise when an essential nutrient is deficient or when there is an imbalance of nutrients. Protein deficiencies and avitaminosis (deficiency of vitamins) are typical examples. An energy deficit leading to cell injury can occur if there is insufficient glucose, or insufficient oxygen to transform the glucose into energy. A lack of insulin, or the inability to use insulin, may also prevent glucose from entering the cell from the

blood. This occurs in diabetes mellitus, a metabolic disorder that can lead to nutritional deficiency.

Physical Agents

Physical agents, including temperature extremes, radiation, electrical shock, and mechanical trauma, can cause injury to the cells or to the entire body. The duration of exposure and the intensity of the stressor determine the severity of damage.

EXTREMES OF HIGH TEMPERATURE

When a person's temperature is elevated, hypermetabolism occurs and the respiratory rate, heart rate, and basal metabolic rate all increase. With fever induced by infections, the hypothalamic thermostat may be reset at a higher temperature, then return to normal when the fever abates. The increase in body temperature is achieved through physiologic mechanisms. Body temperatures greater than 41°C (106°F) suggest hyperthermia, because the physiologic function of the thermoregulatory center breaks down and the temperature soars. This physiologic condition occurs in people with heat stroke. Eventually, the high temperature causes coagulation of cell proteins, and the cells die. The body must be cooled rapidly to prevent brain damage.

The local response to thermal or burn injury is similar. There is an increase in metabolic activity, and, as heat increases, protein is coagulated, enzyme systems are destroyed, and, in the extreme, charring or carbonization occurs. Burns of the epithelium are classified as partial-thickness burns if epithelializing elements remain to support healing. Full-thickness burns lack such elements and must be grafted for healing. The amount of body surface involved determines the prognosis for the patient. If the injury is severe, the entire body system becomes involved, and hypermetabolism develops as a pathophysiologic response.

EXTREMES OF LOW TEMPERATURE

Extremes of low temperature, or cold, cause vasoconstriction. Blood flow becomes sluggish and clots form, leading to ischemic damage in the involved tissues. With still lower temperatures, ice crystals may form, and the cells may burst.

RADIATION AND ELECTRICAL SHOCK

Radiation is used for diagnosis and treatment of diseases. Ionizing forms of radiation may cause injury by their destructive action. Radiation decreases the protective inflammatory response of the cell, creating a favorable environment for opportunistic infections. Electrical shock produces burns as a result of the heat generated when electrical current travels through the body. It may also abnormally stimulate nerves, leading, for example, to fibrillation of the heart.

MECHANICAL TRAUMA

Mechanical trauma can result in wounds that disrupt the cells and tissues of the body. The severity of the wound, the amount of blood loss, and the extent of nerve damage are significant factors in the outcome.

Chemical Agents

Chemical injuries are caused by poisons, such as lye, which has a corrosive action on epithelial tissue, or by heavy metals, such as mercury, arsenic, and lead, each with its own specific destructive action. Many other chemicals are toxic in specific amounts, in certain people, and in distinctive tissues. Excessive secretion of

hydrochloric acid can damage the stomach lining; large amounts of glucose can cause osmotic shifts, affecting the fluid and electrolyte balance; and too much insulin can cause subnormal levels of glucose in the blood (hypoglycemia) and can lead to coma.

Drugs, including prescribed medications, can also cause chemical poisoning. Some individuals are less tolerant of medications than others and manifest toxic reactions at the usual or customary dosages. Aging tends to decrease tolerance to medications. Polypharmacy (taking many medications at one time) also occurs frequently in the aging population and is a problem because of the unpredictable effects of the resulting medication interactions.

Alcohol (ethanol) is also a chemical irritant. In the body, alcohol is broken down into acetaldehyde, which has a direct toxic effect on liver cells that leads to a variety of liver abnormalities, including cirrhosis in susceptible individuals. Disordered liver cell function leads to complications in other organs of the body.

Infectious Agents

Biologic agents known to cause disease in humans are viruses, bacteria, rickettsiae, mycoplasmas, fungi, protozoa, and nematodes. The severity of the infectious disease depends on the number of microorganisms entering the body, their virulence, and the host's defenses (eg, health, age, immune defenses).

Some bacteria, such as those that cause tetanus and diphtheria, produce exotoxins that circulate and create cell damage. Others, such as the gram-negative bacteria, produce endotoxins when they are killed. The tubercle bacillus induces an immune reaction.

Viruses, the smallest living organisms, survive as parasites of the living cells they invade. Viruses infect specific cells. Through a complex mechanism, they replicate within the cells, then invade other cells and continue to replicate. An immune response is mounted by the body to eliminate the viruses, and the cells harboring the viruses can be injured in the process. Typically, an inflammatory response and immune reaction are the physiologic responses of the body to the presence of infection.

Disordered Immune Responses

The immune system is an exceedingly complex system; its purpose is to defend the body from invasion by any foreign object or foreign cell type, such as cancerous cells. This is a steady-state mechanism, but like other adjustment processes it can become disordered, and cell injury will occur. The immune response detects foreign bodies by distinguishing non-self substances from self substances and destroying the non-self entities. The entrance of an antigen (foreign substance) into the body evokes the production of antibodies that attack and destroy the antigen (antigen-antibody reaction).

The immune system can be hypoactive or hyperactive. When it is hypoactive, immunodeficiency diseases occur; when it is hyperactive, hypersensitivity disorders arise. A disorder of the immune system itself can result in damage to the body's own tissues. Such disorders are labeled autoimmune diseases (see Unit 11).

Genetic Disorders

Genetic defects as causes of disease and their effects on genetic structure are of intense research interest. Many of these defects produce mutations that have no recognizable effect, such as lack of a single enzyme; others contribute to more obvious congenital abnormalities, such as Down syndrome. As a result of the Human Genome Project, patients can be genetically assessed for

conditions such as sickle cell disease, cystic fibrosis, hemophilia A and B, breast cancer, obesity, cardiovascular disease, phenylketonuria, and Alzheimer's disease. The availability of genetic information and technology enables health care providers to perform screening, testing, and counseling for patients with genetic concerns. Knowledge obtained from the Human Genome Project has also created opportunities for assessing a person's genetic profile and preventing or treating disease. Diagnostic genetics and gene therapy have the potential to identify and modify a gene before it begins to express traits that would lead to disease or disability.

CELLULAR RESPONSE TO INJURY: INFLAMMATION

Cells or tissues of the body may be injured or killed by any of the agents (physical, chemical, infectious) described earlier. When this happens, an inflammatory response (or inflammation) naturally occurs in the healthy tissues adjacent to the site of injury. **Inflammation** is a defensive reaction intended to neutralize, control, or eliminate the offending agent and to prepare the site for repair. It is a nonspecific response (not dependent on a particular cause) that is meant to serve a protective function. For example, inflammation may be observed at the site of a bee sting, in a sore throat, in a surgical incision, and at a burn site. Inflammation also occurs in cell injury events, such as strokes and myocardial infarctions.

Inflammation is not the same as infection. An infectious agent is only one of several agents that may trigger an inflammatory response. An infection exists when the infectious agent is living, growing, and multiplying in the tissues and is able to overcome the body's normal defenses.

Regardless of the cause, a general sequence of events occurs in the local inflammatory response. This sequence involves changes in the microcirculation, including vasodilation, increased vascular permeability, and leukocytic cellular infiltration (Fig. 6-5). As these changes take place, five cardinal signs of inflammation are produced: redness, heat, swelling, pain, and loss of function.

The transient vasoconstriction that occurs immediately after injury is followed by vasodilation and an increased rate of blood flow through the microcirculation. Local heat and redness result. Next, vascular permeability increases, and plasma fluids (including proteins and solutes) leak into the inflamed tissues, producing swelling. The pain produced is attributed to the pressure of fluids or swelling on nerve endings, and to the irritation of nerve endings by chemical mediators released at the site. Bradykinin is one of the chemical mediators suspected of causing pain. Loss of function is most likely related to the pain and swelling, but the exact mechanism is not completely known.

As blood flow increases and fluid leaks into the surrounding tissues, the formed elements (red blood cells, white blood cells, and platelets) remain in the blood, causing it to become more viscous. Leukocytes (white blood cells) collect in the vessels, exit, and migrate to the site of injury to engulf offending organisms and to remove cellular debris in a process called phagocytosis. Fibrinogen in the leaked plasma fluid coagulates, forming fibrin for clot formation, which serves to wall off the injured area and prevent the spread of infection.

Chemical Mediators

Injury initiates the inflammatory response, but chemical substances released at the site induce the vascular changes. Foremost among these chemicals are histamine and the kinins. Histamine



Physiology/Pathophysiology

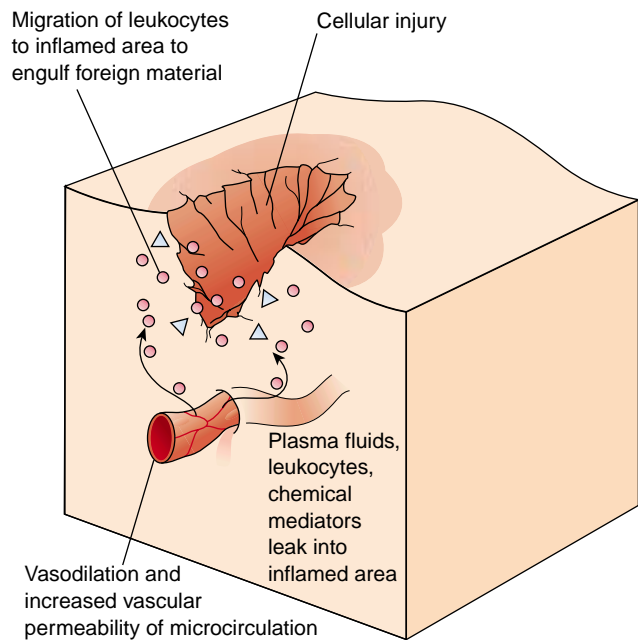


FIGURE 6-5 Inflammatory response. Chemical, physical, infectious, or other factors cause cellular injury. Vasodilation and release of chemical mediators, leukocytes, and proteins occur. Leukocytes remove cellular debris. Fibrinogen and plasma coagulate to prevent spread of infection.

is present in many tissues of the body but is concentrated in the mast cells. It is released when injury occurs and is responsible for the early changes in vasodilation and vascular permeability. Kinins increase vasodilation and vascular permeability; they also attract neutrophils to the area. Prostaglandins, another group of chemical substances, are also suspected of causing increased permeability.

Systemic Response to Inflammation

The inflammatory response is often confined to the site, causing only local signs and symptoms. However, systemic responses can also occur. Fever is the most common sign of a systemic response to injury, and it is most likely caused by endogenous pyrogens (internal substances that cause fever) released from neutrophils and macrophages (specialized forms of leukocytes). These substances reset the hypothalamic thermostat, which controls body temperature, and produce fever. Leukocytosis, an increase in the synthesis and release of neutrophils from bone marrow, may occur to provide the body with greater ability to fight infection. During this process, general, nonspecific symptoms develop, including malaise, loss of appetite, aching, and weakness.

Types of Inflammation

Inflammation is categorized primarily by its duration and the type of exudate produced. It may be acute, subacute, or chronic. Acute inflammation is characterized by the local vascular and exudative changes described earlier and usually lasts less than 2 weeks. An acute inflammatory response is immediate and serves a protective

function. After the injurious agent is removed, the inflammation subsides and healing takes place with the return of normal or near-normal structure and function.

Chronic inflammation develops if the injurious agent persists and the acute response is perpetuated. Symptoms are present for many months or years. Chronic inflammation may also begin insidiously and never have an acute phase. The chronic response does not serve a beneficial and protective function; on the contrary, it is debilitating and can produce long-lasting effects. As the inflammation becomes chronic, changes occur at the site of injury and the nature of the exudate becomes proliferative. A cycle of cellular infiltration, necrosis, and fibrosis begins, with repair and breakdown occurring simultaneously. Considerable scarring may occur, resulting in permanent tissue damage.

Subacute inflammation falls between acute and chronic inflammation. It includes elements of the active exudative phase of the acute response as well as elements of repair, as in the chronic phase. The term subacute inflammation is not widely used.

CELLULAR HEALING

The reparative process begins at approximately the same time as the injury and is interwoven with inflammation. Healing proceeds after the inflammatory debris has been removed. Healing may occur by regeneration, in which gradual repair of the defect occurs by proliferation of cells of the same type as those destroyed, or by replacement, in which cells of another type, usually connective tissue, fill in the tissue defect and result in scar formation.

Healing by Regeneration

The ability of cells to regenerate depends on whether they are labile, permanent, or stable. Labile cells multiply constantly to replace cells worn out by normal physiologic processes; these include epithelial cells of the skin and those lining the gastrointestinal tract. Permanent cells include neurons—the nerve cell bodies, not their axons. Destruction of a neuron is a permanent loss, but axons may regenerate. If normal activity is to return, tissue regeneration must occur in a functional pattern, especially in the growth of several axons. Stable cells have a latent ability to regenerate. Under normal physiologic processes, they are not shed and do not need replacement, but if they are damaged or destroyed, they are able to regenerate. These include functional cells of the kidney, liver, and pancreas.

Healing by Replacement

Depending on the extent of damage, tissue healing may occur by primary intention or by secondary intention. In primary intention healing, the wound is clean and dry and the edges are approximated, as in a surgical wound. Little scar formation occurs, and the wound is usually healed in a week. In secondary intention healing, the wound or defect is larger and gaping and has necrotic or dead material. The wound fills from the bottom upward with granulation tissue. The process of repair takes longer and results in more scar formation, with loss of specialized function. People who have recovered from myocardial infarction, for example, have abnormal electrocardiographic (ECG) tracings because the electrical signal cannot be conducted through the connective tissue that has replaced the infarcted area.

The condition of the host, the environment, and the nature and severity of the injury affect the processes of inflammation and

repair. Any of the injuries previously discussed can lead to death of the cell. Essentially, the cell membrane becomes impaired, resulting in a nonrestricted flow of ions. Sodium and calcium enter the cell, followed by water, which leads to edema, and energy transformation ceases. Nerve impulses are no longer transmitted; muscles no longer contract. As the cells rupture, lysosomal enzymes that destroy tissues escape, and cell death and necrosis occur.

NURSING IMPLICATIONS

In the assessment of the person who seeks health care, both objective signs and subjective symptoms are the primary indicators of the physiologic processes that are occurring. The following questions are addressed during the assessment:

- Are the heart rate, respiratory rate, and temperature normal?
- What emotional distress may be contributing to the patient's health problems?
- Are there other indicators of steady-state deviation?
- What is the person's blood pressure, height, and weight?
- Are there any problems in movement or sensation?
- Does the person demonstrate any problems with affect, behavior, speech, cognitive ability, orientation, or memory?
- Are there obvious impairments, lesions, or deformities?

Further signs of change are indicated in diagnostic studies such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). Objective evidence can also be obtained from laboratory data, including electrolytes, blood urea nitrogen (BUN), blood glucose, and urinalysis.

In making a nursing diagnosis, the nurse must relate the symptoms or complaints expressed by the patient to the physical signs that are present. Management of specific biologic disorders is discussed in subsequent chapters; however, the nurse can assist any patient to respond to stress-inducing biologic or psychological disorders with stress-management interventions.

Stress Management: Nursing Interventions

Stress or the potential for stress is ubiquitous; that is, it is everywhere and anywhere at once. Anxiety, frustration, anger, and feelings of inadequacy, helplessness, or powerlessness are emotions often associated with stress. In the presence of these emotions, the customary activities of daily living may be disrupted; for example, a sleep disturbance may be present, eating and activity patterns may be altered, and family processes or role performance may be disrupted.

Many nursing diagnoses are possible for patients suffering from stress. One nursing diagnosis related to stress is Anxiety, which is defined as a vague, uneasy feeling, the source of which may be nonspecific or not known to the person. Stress may also be manifested as ineffective coping patterns, impaired thought processes, or disrupted relationships. These human responses are reflected in the nursing diagnoses of Impaired adjustment, Ineffective coping, Defensive coping, and Ineffective denial, all of which indicate poor adaptive responses. Other possible nursing diagnoses include Social isolation, Risk for impaired parenting, Spiritual distress, Readiness for family coping, Decisional conflict, Situational low self-esteem, and Powerlessness, among others. Because human responses to stress are varied, as are the sources of stress, arriving at an accurate diagnosis allows interventions and goals to be more specific and leads to improved outcomes.

Stress management is directed toward reducing and controlling stress and improving coping. Nurses might use these methods not only with their patients but also in their own lives. The need to prevent illness, improve the quality of life, and decrease the cost of health care makes efforts to promote health essential, and stress control is a significant health-promotion goal. Stress-reduction methods and coping enhancements can derive from either internal or external sources. For example, adopting healthy eating habits and practicing relaxation techniques are internal resources that help to reduce stress; developing a broad social network is an external resource that helps reduce stress. Goods and services that can be purchased are also external resources for stress management, and it is much easier for individuals with adequate financial resources to cope with constraints in the environment, because their sense of vulnerability to threat is decreased.

PROMOTING A HEALTHY LIFESTYLE

An individual's personal resources that aid in coping include health and energy. A health-promoting lifestyle provides these resources and buffers or cushions the impact of stressors. Lifestyles or habits that contribute to the risk of illness can be identified through a health risk appraisal.

A health risk appraisal is an assessment method that is designed to promote health by examining an individual's personal habits and recommending changes when a health risk is identified. Health risk questionnaires estimate the likelihood that a person with a given set of characteristics will become ill. It is hoped that if people are provided with this information, they will alter their activities (eg, stop smoking, have periodic screening examinations) to improve their health. Questionnaires typically address the following information:

1. Demographic data: age, sex, race, ethnic background
2. Personal and family history of diseases and health problems
3. Lifestyle choices
 - a. Eating, sleeping, exercise, smoking, drinking, sexual activity, and driving habits
 - b. Stressors at home and on the job
 - c. Role relationships and associated stressors
4. Physical measurements
 - a. Blood pressure
 - b. Height, weight
 - c. Laboratory analyses of blood and urine
5. Participation in high-risk behaviors

The personal information is compared with average population risk data, and the risk factors are identified and weighted. From this analysis, the person's risks and major health hazards are identified. Further comparisons with population data can estimate how many years will be added to the person's life span if the suggested changes are made. However, research so far has not demonstrated that providing people with such information ensures that they will change their habits. The single most important factor for determining health status is social class, and within a social class the research suggests that the major factor influencing health is level of education (Mickler, 1997).

ENHANCING COPING STRATEGIES

McCloskey and Bulechek (1999) identified "coping enhancement" as a nursing intervention and defined it as "assisting a patient to adapt to perceived stressors, changes, or threats that interfere with meeting life demands and roles" (Chart 6-2). The

nurse can build on the patient's existing coping strategies, as identified in the health appraisal, or teach new strategies for coping if necessary.

The five predominant ways of coping with illness identified in a review of 57 nursing research studies were as follows (Jalowiec, 1993):

- Trying to be optimistic about the outcome
- Using social support
- Using spiritual resources
- Trying to maintain control either over the situation or over feelings
- Trying to accept the situation

Other ways of coping included seeking information, reprioritizing needs and roles, lowering expectations, making compromises, comparing oneself to others, planning activities to conserve energy, taking things one step at a time, listening to one's body, and using self-talk for encouragement.

The nurse can implement the coping enhancement interventions and explore methods for improving the patient's coping abilities.

TEACHING RELAXATION TECHNIQUES

Relaxation techniques are a major method used to relieve stress. Commonly used techniques include progressive muscle relaxation, the Benson Relaxation Response, and relaxation with guided imagery. The goal of relaxation training is to produce a response that counters the stress response. When this goal is achieved, the action of the hypothalamus adjusts and decreases the activity of the sympathetic and parasympathetic nervous systems. The sequence of physiologic effects and their signs and symptoms are interrupted, and psychological stress is reduced. This is a learned response and requires practice to achieve.

The different relaxation techniques share four similar elements: (1) a quiet environment, (2) a comfortable position, (3) a passive attitude, and (4) a mental device (something on which to focus the attention, such as a word, phrase, or sound).

Progressive Muscle Relaxation

Progressive muscle relaxation involves tensing and releasing the muscles of the body in sequence and sensing the difference in feeling. It is best if the person lies on a soft cushion on the floor, in a quiet room, breathing easily. Someone usually reads the instructions in a low tone and with a slow and relaxed manner, or a tape of the instructions may be played. The person tenses the muscles in the whole body (one muscle group at a time), holds, senses the tension, and then relaxes. As each muscle group is tensed, the person keeps the rest of the body relaxed. Each time the focus is on feeling the tension and relaxation. When the exercise is completed, the whole body should be relaxed (Benson, 1993; Benson & Stark, 1996).

Benson's Relaxation Response

Benson (1993) describes the following steps of the Benson Relaxation Response:

1. Pick a brief phrase or word that reflects your basic belief system.
2. Choose a comfortable position.
3. Close your eyes.
4. Relax your muscles.

5. Become aware of your breathing, and start using your selected focus word.
6. Maintain a passive attitude.
7. Continue for a set period of time.
8. Practice the technique twice daily.

This response combines meditation with relaxation. Along with the repeated word or phrase, a passive attitude is essential. If other thoughts or distractions (noises, the pain of an ailment) occur, Benson recommends not fighting the distraction but simply continuing to repeat the focus phrase. The time of day is not important, but the exercise works best on an empty stomach.

Relaxation With Guided Imagery

Simple **guided imagery** is the “purposeful use of imagination to achieve relaxation or direct attention away from undesirable sensations” (McCloskey & Bulechek, 1999, p. 506). The nurse helps the person select a pleasant scene or experience, such as watching the ocean or dabbling the feet in a cool stream. This image serves as the mental device in this technique. As the person sits comfortably and quietly, the nurse guides the individual to review the

scene, trying to feel and relive the imagery with all of the senses. A tape recording may be made of the description of the image, or commercial tape recordings for guided imagery and relaxation can be used.

Other relaxation techniques include meditation, breathing techniques, massage, Reiki, music therapy, biofeedback, and the use of humor.

EDUCATING

Two commonly prescribed nursing educational interventions—providing sensory information and providing procedural information (eg, preoperative teaching)—have the goal of reducing stress and improving the patient’s coping ability. This preparatory education includes giving structured content, such as a lesson in childbirth preparation to expectant parents, a review of cardiovascular anatomy to the cardiac patient, or a description of sensations the patient will experience during cardiac catheterization. These techniques may alter the person–environment relationship such that something that might have been viewed as harmful or a threat will now be perceived more positively. Giving patients information also reduces the emotional response so

that they can concentrate and solve problems more effectively (Calvin & Lane, 1999; Millo & Sullivan, 2000).

ENHANCING SOCIAL SUPPORT

The nature of social support and its influence on coping have been studied extensively; social support has been demonstrated to be an effective moderator of life stress. Social support has been found to provide the individual with several different types of emotional information (Heitzman & Kaplan, 1988; Wineman, 1990). The first type of information leads people to believe that they are cared for and loved. This emotional support appears most often in a relationship between two people in which mutual trust and attachment are expressed by helping one another meet their emotional needs. The second type of information leads people to believe that they are esteemed and valued. This is most effective when there is recognition that demonstrates the individual's favorable position in the group. It elevates the person's sense of self-worth and is called esteem support. The third type of information leads people to believe that they belong to a network of communication and mutual obligation. Members of this network share information and make goods and services available to the members on demand.

Social support also facilitates an individual's coping behaviors; this depends, however, on the nature of the social support. People can have extensive relationships and interact frequently, but the necessary support comes only when there is a deep level of involvement and concern, not when people merely touch the surface of each other's lives. The critical qualities within a social network are the exchange of intimate communications and the presence of solidarity and trust.

Emotional support from family and significant others provides a person with love and a sense of sharing the burden. The emotions that accompany stress are unpleasant and often increase in a spiraling fashion if relief is not provided. Being able to talk with someone and express feelings openly may help the person to gain mastery of the situation. Nurses can provide this support; however, it is important to identify the person's social support system and encourage its use. People who are loners, who are isolated, or who withdraw in times of stress have a high risk of coping failure.

Because anxiety can also distort a person's ability to process information, it helps to seek information and advice from others who can assist with analyzing the threat and developing a strategy to manage it. Again, this use of others helps the person to maintain mastery of a situation and to retain self-esteem.

Thus, social networks assist with management of stress by providing the individual with

- A positive social identity
- Emotional support
- Material aid and tangible services
- Access to information
- Access to new social contacts and new social roles

RECOMMENDING SUPPORT AND THERAPY GROUPS

Support groups exist especially for people in similar stressful situations. Groups have been formed by parents of children with leukemia, people with ostomies, mastectomy patients, and those with other kinds of cancer or other serious diseases, chronic illnesses, and disabilities. There are groups for single parents, sub-

stance abusers and their family members, and victims of child abuse. Professional, civic, and religious support groups are active in many communities. There are also encounter groups, assertiveness training programs, and consciousness-raising groups to help people modify their usual behaviors in their transactions with their environment. Being a member of a group with similar problems or goals has a releasing effect on a person that promotes freedom of expression and exchange of ideas.

As previously noted, a person's psychological and biologic health, internal and external sources of stress management, and relationships with the environment are predictors of health outcomes. These factors are directly related to the health patterns of the individual. The nurse has a significant role and responsibility in identifying the health patterns of the person receiving care. If those patterns are not achieving physiologic, psychological, and social balance, the nurse is obligated, with the assistance and agreement of the patient, to seek ways to promote balance.

Although this chapter has presented some physiologic mechanisms and perspectives on health and disease, the way that one copes with stress, the way one relates to others, and the values and goals held are also interwoven into those physiologic patterns. To evaluate a patient's health patterns and to intervene if a problem exists requires a total assessment of the person. Specific problems and their nursing management are addressed in greater depth in other chapters.



Critical Thinking Exercises

1. Think about a patient who has survived a major motor vehicle crash and is hospitalized for severe burns, a fractured hip, and multiple lacerations and abrasions. Identify the actual and potential physical, physiological, and psychosocial stressors evident from this person's trauma. Determine nursing strategies to reduce or alleviate these stressors.
2. A 50-year-old woman is diagnosed with osteoporosis after sustaining a rib fracture. The nurse is evaluating the coping style of the woman. What indications would the nurse note in her interactions and follow-up care for this patient that demonstrate that the woman uses problem-focused coping and emotion-focused coping?
3. Select a patient to whom you are assigned who has an acute illness or injury. Describe the manner in which homeostasis has been maintained or disrupted and the compensatory mechanisms that are evident. How does the patient's medical treatment support the compensatory mechanisms? How do you determine the nursing interventions that are appropriate for promoting the healing process?
4. A family composed of two parents, two adolescent male sons, and the maternal grandfather explore with the nurse their health promotion needs. The family's health history reveals that the mother has adult-onset diabetes; the father has coronary artery disease; the sons are somewhat overweight; and the grandfather has mild congestive heart failure. The family has ample resources for making changes in their lifestyle. What interventions would the nurse initiate to promote a healthier lifestyle for this family?

REFERENCES AND SELECTED READINGS

Books

- Andreoli, T. E. (Ed.). (1997). *Cecil essentials of medicine* (4th ed.). Philadelphia: W. B. Saunders.
- Barnfather, J. S., & Lyon, B. L. (Eds.). (1993). *Stress and coping: State of the science and implications for nursing theory, research and practice*. Indianapolis: Sigma Theta Tau International Inc.
- Benson, H. (1993). The relaxation response. In D. Goleman & J. Gurin (Eds.), *Mind-body medicine: How to use your mind for better health* (pp. 125–148). Yonkers, NY: Consumer Reports Books.
- Benson, H., & Proctor, W. (1984). *Beyond the relaxation response*. New York: Berkley Books.
- Benson, H., & Stark, M. (1996). *Timeless healing*. New York: Scribner.
- Copel, L. C. (2000). *Nurse's clinical guide: Psychiatric and mental health care* (2nd ed.). Springhouse, PA: Springhouse.
- Dubos, R. (1965). *Man adapting*. New Haven, CT: Yale University Press.
- Fauci, A. (Ed.). (1998). *Harrison's principles of internal medicine* (14th ed.). New York: McGraw-Hill.
- Guyton, A. C. (1996). *Human physiology: Mechanisms of disease* (6th ed.). Philadelphia: W. B. Saunders.
- Guyton, A. C. (1995). *Textbook of medical physiology* (9th ed.). Philadelphia: W. B. Saunders.
- Jalowiec, A. (1993). Coping with illness: Synthesis and critique of the nursing literature from 1980–1990. In J. S. Barnfather & B. L. Lyon (Eds.), *Stress and coping: State of the science and implications for nursing theory, research and practice*. Indianapolis: Sigma Theta Tau International Inc.
- Lazarus, R. S. (1991a). *Emotion and adaptation*. New York: Oxford University Press.
- Lazarus, R. S. (1993). Why we should think of stress as a subset of emotion. In L. Goldberger & S. Breznitz (Eds.), *Handbook of stress* (2nd ed.). New York: The Free Press.
- Lazarus, R. S., & Folkman, S. (1984). *Stress, appraisal, and coping*. New York: Springer Publishing Co.
- McCloskey, J. C., & Bulechek, G. M. (Eds.). (1999). *Nursing interventions classification (NIC)* (2nd ed.). St. Louis: Mosby-Year Book.
- McEwen, B., & Mendelson, S. (1993). Effects of stress on the neurochemistry and morphology of the brain: Counterregulation versus damage. In I. Goldberger & S. Breznitz (Eds.), *Handbook of stress* (2nd ed.). New York: The Free Press.
- Mickler, M. (1997). *Community organizing and community building for health*. New Brunswick, NJ: Rutgers University Press.
- Miller, L. H., & Smith, A. D. (1993). *The stress solution*. New York: Pocket Books.
- North American Nursing Diagnosis Association. (2000). *NANDA nursing diagnoses: Definitions and classifications*. Philadelphia: Author.
- Selye, H. (1976). *The stress of life*. (Rev. ed.). New York: McGraw-Hill.
- Watkins, A. (Ed.). (1997). *Mind-body medicine: A clinician's guide to psychoneuroimmunology*. New York: Churchill Livingstone.

Journals

Asterisks indicate nursing research articles.

- *Almberg, B., Grafstrom, M., & Winblad, B. (1997). Major strain and coping strategies as reported by family members who care for aged demented relatives. *Journal of Advanced Nursing*, 26(4), 683–691.
- Anderson, B. L., Farrar, W. B., Golden-Kreutz, D., et al. (1998). Stress and immune responses after surgical treatment for regional breast cancer. *Journal of National Cancer Institute*, 90(1), 30–36.
- Baird, C. L. (2000). Living with hurting and difficulty doing: Older women with osteoarthritis. *Clinical Excellence for Nurse Practitioners*, 4(4), 231–237.
- Ballard, A. (1981). Identification of environmental stressors for patients in a surgical intensive care unit. *Issues in Mental Health Nursing*, 11(3), 89–100.
- Biondi, M., Peronti, M., Pacitti, F., Pancheri, P., Pacifici, R., Altieri, I., Paris, L., & Zuccaro, P. (1994). Personality, endocrine and immune changes after eight months in healthy individuals under normal daily stress. *Psychotherapy and Psychosomatics*, 62(3–4), 176–184.
- Black, P. H. (1994). Central nervous system–immune system interactions: Psychoneuroendocrinology of stress and its immune consequences. *Antimicrobial Agents and Chemotherapy*, 38(1), 1–6.
- *Brillhart, B., & Johnson, K. (1997). Motivation and the coping process of adults with disabilities: A qualitative study. *Rehabilitation Nursing*, 22(5), 249–256.
- Bryla, C. M. (1996). The relationship between stress and the development of breast cancer: A literature review. *Oncology Nursing Forum*, 23(3), 441–448.
- Calvin, R. L., & Lane, P. L. (1999). Perioperative uncertainty and state anxiety of orthopedic surgical patients. *Orthopaedic Nursing*, 18(6), 61–66.
- Chalfont, L., & Bennett, P. (1999). Personality and coping: Their influence on affect and behavior following myocardial infarction. *Coronary Health Care*, 3(3), 110–116.
- Clements, K., & Turpin, G. (2000). Life events exposure, physiological reactivity, and psychological strain. *Journal of Behavioral Medicine*, 23(1), 73–94.
- Cohen, J. I. (2000). Stress and mental health: A biobehavioral perspective. *Issues in Mental Health Nursing*, 21(2), 185–202.
- *Collins, M. A. (1996). The relation of work stress, hardiness, and burnout among full-time hospital staff nurses. *Journal of Nursing Staff Development*, 12(2), 81–85.
- *Constantino, R. E., Sekula, L. K., Rabin, B., & Stone, C. (2000). Negative life experiences, depression, and immune function in abused and non-abused women. *Biological Research in Nursing*, 1(3), 190–198.
- Cronquist, A., Wredde, R., Norlander, R., Langius, A., & Bjorvell, H. (2000). Perceived discomfort and related coping phenomenon in patients undergoing percutaneous transluminal coronary angioplasty. *Coronary Health Care*, 4(3), 123–129.
- *Fallon, M., Gould, D., & Wainwright, S. P. (1997). Stress and quality of life in the renal transplant patient: A preliminary investigation. *Journal of Advanced Nursing*, 25(3), 562–570.
- *Felton, B. S. (2000). Resilience in a multicultural sample of community-dwelling women older than age 85. *Clinical Nursing Research*, 9(2), 102–103.
- Glaser, R., & Kiecolt-Glaser, J. K. (1997). Chronic stress modulates the virus-specific immune response to latent herpes simplex virus type 1. *Annals Behavioral Medicine*, 19(2), 78–82.
- Goodkin, K., Feaster, D. J., Tuttle, R., Blaney, N. T., Kumar, M., Baum, M. K., Shapshak, P., & Fletcher, M. A. (1996). Bereavement is associated with time-dependent decrements in cellular immune function in asymptomatic human immunodeficiency virus type 1-seropositive homosexual men. *Clinics in Diagnostic Laboratory Immunology*, 3(1), 109–180.
- *Hagerty, B. M., Williams, R. A., Coyne, J. C., & Early, M. R. (1996). Sense of belonging and indicators of social and psychological functioning. *Archives of Psychiatric Nursing*, 10(4), 235–244.
- Heitzman, C. A., & Kaplan, R. M. (1998). Assessment of methods for measuring social support. *Health Psychology*, 7, 75–109.
- Holmes, T. H., & Rahe, R. H. (1967). The social readjustment rating scale. *Journal of Psychosomatic Research*, 11, 213–218.
- *Kennedy, J. W. (2000). Women's inner balance: A comparison of stressors, personality traits, and health problems by age groups. *Journal of Advanced Nursing*, 31(3): 639–650.
- *Langford, C. P., Bowsher, J., Maloney, J. P., & Lillis, P. P. (1997). Social support: A conceptual analysis. *Journal of Advanced Nursing*, 25(1), 95–100.
- Lazarus, R. S. (1991b). Cognition and motivation in emotion. *American Psychologist*, 46(4), 352–367.
- Lazarus, R. S. (1991c). Progress on a cognitive-motivational-relational theory of emotion. *American Psychologist*, 46(8), 819–834.
- *Mahat, G. (1997). Perceived stressors and coping strategies among individuals with rheumatoid arthritis. *Journal of Advanced Nursing*, 25(6), 1144–1150.
- Mathews, K. A., Caggiula, A. R., McAllister, C. G., et al. (1995). Sympathetic reactivity to acute stress and immune response in women. *Psychosomatic Medicine*, 57(6), 564–571.

- *Millio, M. E., & Sullivan, K. (2000). Patients with operable esophageal cancer: Their experience of information giving in a regional thoracic unit. *Journal of Clinical Nursing*, 9(2), 236–246.
- Morse, D. L. (2000). Continuing care extra: Relocation stress is real. *American Journal of Nursing*, 100(8), 24A–24D.
- *Morse, S. R., & Fife, B. (1998). Coping with a partner's cancer, adjustment at four stages of the illness trajectory. *Oncology Nursing Forum*, 25(4), 751–760.
- Pike, J. L., Smith, T. L., Hauger, R. L., et al. (1997). Chronic life stress alters sympathetic, neuroendocrine, and immune responsivity to an acute psychological stressor in humans. *Psychosomatic Medicine*, 59(4), 447–457.
- Robinson, F. P., Matthews, H. L., Witek-Janusek, L. (2000). Stress reduction and HIV disease: A review of intervention studies using a psychoimmunology framework. *Journal of the Association of Nurses in AIDS Care*, 11(2), 87–96.
- *Ryan, M. C. (1996). Loneliness, social support and depression as interactive variables with cognitive status: testing Roy's model. *Nursing Science Quarterly*, 9(3), 107–114.
- Schrader, K. A. (1996). Stress and immunity after traumatic injury: The mind–body link. *AACN Clinical Issues in Critical Care Nursing*, 7(3), 351–358.
- Seers, K., & Carrol, D. (1998). Relaxation techniques for acute pain management: A systematic review. *Journal of Advanced Nursing*, 27(3), 466–475.
- Sergerstrom, S. C., Fahey, J. L., Kemeny, M. E., & Taylor, S. E. (1998). Optimism is associated with mood, coping, and immune change in response to stress. *Journal of Perspectives in Social Psychology*, 74(6), 1646–1655.
- Smith, L. L. (2000). Cytokine hypothesis of overtraining: A physiological adaptation to excessive stress? *Medicine and Science in Sports and Exercise*, 32(2), 317–331.
- *Starzonski, R., & Hilton, A. (2000). Patient and family adjustment to kidney transplantation with and without an interim period of dialysis. *Nephrology Nursing Journal*, 27(1), 17, 18, 21–33, 52.
- Tausig, M. (1982). Measuring life events. *Journal of Health and Social Behavior*, 23(1), 52–64.
- Wells-Federman, C. (1996). Awakening the nurse healer within. *Holistic Nursing Practice*, 10(2), 13–29.
- *Williams, A. M. (2000). Distress and hardiness: A comparison of African Americans and white caregivers. *Journal of National Black Nurses Association*, 11(1), 21–26.
- *Wineman, N. M. (1990). Adaptation to multiple sclerosis: The role of social support, functional disability, and perceived uncertainty. *Nursing Research*, 39, 294–299.