Pathophysiology

An Introduction to the Mechanisms of Disease

BERNICE L. MUIR

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AN INTRODUCTION TO THE MECHANISMS OF DISEASE

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Preface

Some schools of nursing have taken the pathophysiology out of their nursing courses and offer it as a separate support course so that nursing courses can put more emphasis on nursing measures. I taught such a separate pathophysiology course at Cariboo College for two years. During that time I could not find a suitable pathophysiology book to adopt as a course text but had to draw material from many different sources. Therefore, with the urging of several of my colleagues and some of my students, I decided to write this pathophysiology textbook.

Most of the books that are currently available follow the medical model, organ system by organ system, and are oriented to specific diseases. Many nursing programs no longer follow the medical model, however, but base their curricula on the adaptation model or needs model. The purpose of this book is to present broad principles in an integrated manner, which cannot be done using an organ system approach. The focus is on mechanisms by which pathogenic agents disrupt homeostasis and mechanisms by which the body maintains or restores homeostasis. The intent is not to cover every disease, although many specific diseases are given as examples. My philosophy is to include sufficient facts and details to enable students to *understand* the mechanisms and principles involved, rather than to merely provide a list of signs and symptoms for them to *memorize*.

It is expected that the students using this book have had a previous course in anatomy and physiology. I have included a review of normal physiology in some sections, however, particularly in areas where I feel students may have difficulty understanding the pathophysiological concepts if they do not have a firm grounding in normal physiology. I expect that the people using this book have different levels of background knowledge. Therefore I have started each chapter or section with relatively simple explanations and definitions and proceeded from there to cover the topic in increasing depth. Those with more advanced levels of prior knowledge may wish to skip the beginning sections in each chapter, but I suspect many students will appreciate the review, even if they have learned the material previously.

I have placed considerable emphasis on genetics in this book, because diseases with a genetic component are assuming greater importance as infectious diseases and nutritional deficiency come under control. Since many nursing programs do not include a genetics course, two chapters are devoted to basic principles of genetics. On the other hand, I have not ignored infectious diseases or nutritional aspects of disease. In the discussion of infectious diseases, however, the emphasis is on general principles of host-microbe interactions rather than specific microorganisms and specific diseases. I have not included a separate discussion of aging, because I consider aging to be a normal process, not a pathophysiological one. Where pertinent, however, age-related aspects of disease have been discussed and all age groups have been covered.

This book can be used as a textbook for a separate pathophysiology course such as I taught or as a reference text where pathophysiology is integrated into a nursing course. The pathophysiological concepts presented here can provide the bases for subsequent nursing actions, although the application to nursing is not included in this book. In Unit One, I have attempted to point out that physiological processes represent only one aspect of a person. It is beyond the scope of this book, however, to include the many psychological, social, and cultural factors that influence individual responses. I leave it to nursing faculty to help students integrate the material in this text with knowledge learned from other courses and apply it to the nursing process.

Bernice L. Muir

Acknowledgments

Having never written a book before, I started on the adventure of writing this one thinking I was climbing a small mountain; when I got part way up the slope, I discovered it was Mt. Everest. I could not have reached the peak without the support, encouragement, and assistance of my family and friends. I am deeply indebted to all of them. I would especially like to thank Beverley Green, Valerie Macdonald, Hazel Thomas, my sister Shirley, and my parents. The help and encouragement of former colleagues Dawn Patterson, Claudette Kelly, and Pam Steuart was also greatly appreciated.

Several people offered suggestions and criticisms as the book was being written; I appreciated the comments, even if I did not always follow the advice. In addition, I am indebted to the people who generously provided the photographs that appear in this book. Specific credit is cited where the illustrations appear.

My typist, Louise Hunter, deserves special thanks, not only for doing an excellent job of typing and retyping the manuscript but also for rendering services above and beyond the call of duty. I would also like to thank her husband, Bob, who helped check the manuscript for typographical errors and thought of the "please sign here" example for Chapter 3.

I should also like to thank the staff at Wiley. I am particularly grateful to Cathy Somer, Nursing Editor, for her kind and patient help and encouragement.

Contents

UNIT ONE

BASIC CONCEPTS OF HEALTH AND DISEASE

1 Homeostasis and Adaptation

All living cells must exchange substances with their environment. Nutrients are taken into cells and wastes are eliminated. Respiratory gases are exchanged. For unicellular organisms these exchanges occur directly with the surrounding environment, but in complex multicellular organisms, such as human beings, relatively few cells are in direct contact with the external environment. The interior cells still require nutrients and still must eliminate wastes. They need oxygen and must be rid of carbon dioxide. Internal cells cannot carry out this exchange directly with the outer world. They must have some intermediate means of exchanging substances with the external environment in which the whole organism exists.

The spaces between the body cells contain *extracellular fluid* (i.e., fluid outside the cells), which bathes the cells and provides a medium for the exchange of nutrients and wastes. A 19th-century French physiologist, Claude Bernard, developed the concept that the body fluids that immediately surround the cells form the *internal environment* (milieu intérieur) of complex organisms. The specialized functions of the various organ systems of the body provide the means of exchange between this internal environment and the external environment. Thus, nutrients from the external environment are absorbed via the gastrointestinal tract; soluble wastes are excreted through the kidneys; and the lungs provide the means of exchange of respiratory gases. The circulatory system serves to transport and distribute substances throughout the internal environment. It is with this internal environment, then, that the body cells interact.

HOMEOSTASIS

Bernard not only developed the concept of the internal environment but also recognized that conditions in the internal environment remain relatively constant. The concentration of nutrients, for example glucose, in the extracellular fluid is fixed within certain limits. Waste products are normally eliminated from the body as rapidly as they are formed, so that their concentration does not exceed limits that would be toxic to the cells. The level of respiratory gases is kept within a limited range. Acidity, salt concentration, osmotic pressure, and temperature are other characteristics of the human internal environment that are kept constant. Bernard realized that for optimum functioning of the cells, these physicochemical properties of the body fluids can fluctuate only within very narrow limits. He explained that the major objective of all the vital mechanisms is to preserve constant conditions of life in the internal environment.

A number of scientists since Claude Bernard have contributed their ideas to the concept that a constant and optimal internal environment is necessary for normal body function. In 1926 an American physiologist, W. B. Cannon, introduced the term *homeostasis* to denote the maintenance of constant conditions in the internal environment. The word is derived from the Greek word roots *homeo*, meaning like or similar, and *stasis*, meaning standing. The term homeostasis encompasses not only the idea of internal constancy or stability but also includes the concept that coordinated body processes are responsible for maintaining the constancy of the internal environment. This constancy should not be viewed as a stagnant thing: it is dynamic. Substances are continually being added to the internal environment and being taken away from it, but the net result is relatively constant. There is variation, but only within narrow limits.

A stable internal environment is necessary for the survival of every cell in the body. In addition to carrying out the basic activities necessary for maintaining its own life, each cell performs some specialized function. This specialized function, together with the activities of other cells, contributes to the constancy of the extracellular fluid. The survival of the total organism, as well as the survival of each cell, depends on the concerted cellular activities that maintain homeostasis. Integration and coordination of these activities is brought about by the nervous system and the endocrine system.

Physiologically, the term *internal environment* refers to the extracellular fluid. The term is also used in a broader context, however, to denote everything inside the skin and mucous membranes. In this context the internal environment is said to consist not only of physiological (or physical) elements but also psychological and sociocultural elements. These elements interact with each other and with their counterparts in the external environment. Similarly, the term homeostasis has been broadened from its original physiological context and is used to denote stability of all aspects of the individual: physiological, psychological, and sociocultural. In other words, homeostasis refers to the stability of the total organism. Sometimes the term homeostasis is used to refer to the self-stabilizing tendency of societies as well as individuals. In this textbook the terms internal environment and homeostasis are used primarily in the physiological sense. It is important to realize, however, that psychological and sociocultural factors influence physiological responses, because an individual is an integrated being.

Maintenance of Homeostasis

Changes in the external environment may produce fluctuations in the internal environment if the organism does not have some means of compensating. Similarly, activities of the individual will produce disturbances in the internal environment. These disturbances must be counteracted in order to maintain homeostasis. For example, fluctuations in the temperature of the external environment and varying degrees of muscular activity, which produce heat within the individual, would tend to alter body temperature if there were no mechanism for temperature regulation.

Maintenance of homeostasis also depends on satisfaction of basic needs. Physiologically these needs include, for example, intake of oxygen, nutrients, and water, and elimination of carbon dioxide and wastes. The amount of oxygen, nutrients, and water required and the quantity of carbon dioxide and wastes to be eliminated will depend on the activity of the individual. Meeting the need for oxygen, nutrients, and water will depend not only on their availability in the external environment but also on the ability of the organism to take them into the internal environment. Therefore, to maintain homeostasis the organism must have mechanisms to compensate for varying demands made on the body. Thus, for example, during exercise the rate of pulmonary ventilation is increased to meet the demand for more oxygen and to eliminate the increased amount of carbon dioxide that is produced. At high altitudes where oxygen availability is decreased, the body responds with increased production of red blood cells, which increases the oxygen-carrying capacity of the blood and facilitates oxygen uptake. The nature of the mechanisms by which the body adjusts to varying demands and counteracts changes is discussed in the section on Homeostatic Mechanisms.

The physical integrity of the organism must be preserved in order to maintain homeostasis. For example, every organism has a surface membrane that forms a barrier between the internal and external environments. In the case of a unicellular organism such as an ameba, the surface membrane is the cell membrane. In human beings the cutaneous membrane on the outside and the mucous membranes lining ducts and body cavities that open to the exterior form the barrier between the internal and external environments. Disruption of the surface membrane will impair the ability of the organism to regulate the exchange of substances between the two environments. Noxious elements from outside may enter the organism, and vital elements from inside may be lost. In order to maintain physical integrity the organism must have mechanisms to protect itself from injury, as well as mechanisms to repair any damage that is done. For example, the body has many protective reflexes, such as blinking if an object comes near the eyes or withdrawing a limb from a painful stimulus. If a blood vessel is damaged, clotting occurs to prevent blood loss. This subject is the topic of Chapter 7. The wound-healing mechanism repairs damage to tissues. This mechanism is described in Chapter 8.

Maintenance of homeostasis involves various forms of adjustment by the organism in response to actual or threatened disturbances in the internal environment. These disturbances may arise from within the individual or may be due to changes in the external environment.

ADAPTATION

The process of adjusting to environmental conditions is called *adaptation*. Adaptability is a characteristic of all living organisms, not only of human beings. Adaptation is necessary for survival. The term adaptation is used in a number of contexts, each with a slightly different meaning.

Adaptation by Species and Groups

Evolutionary Adaptation

Evolutionary adaptation refers to the process of modification of the genetic constitution of populations through natural selection. In this process, when the external environment of a species is altered over a long period of time, only those individuals most suited to the changed environmental conditions are able to survive and reproduce (and consequently to pass along genetic information to the next generation). The genes that code for the advantageous characteristics become fixed in the population, while genes that code for disadvantageous characteristics are lost. All the inherited anatomical, physiological, and behavioral characteristics of present populations are the result of evolutionary adaptation acting on the ancestral populations of the species. A classic example of evolutionary adaptation is the emergence of a dark form of a particular species of moth in England. Before the industrial revolution, the usual form of the moth was speckled white. Occasionally mutant forms that were much darker would occur. Now in industrialized areas where smoke and soot from factories darken the bark of trees, the dark form of the moth is predominant. The dark moths are hardly visible against the darkened tree trunks and so are not eaten by birds. The light-colored moths stand out against the dark background and are eaten by predators. In nonpolluted areas, however, the light form is still predominant.

Cultural Adaptation

Cultural adaptation denotes the behavioral adjustments of groups of people (societies) to changing conditions of life associated with the processes of civilization. Cultural adaptation occurs almost exclusively in human beings. It depends on the ability of humans to learn from previous experiences, to accumulate knowledge acquired by the members of society, and to transmit this knowledge to other people and to succeeding generations. The processes of cultural adaptation are not genetically transmitted, but they are dependent upon the genetically determined potential of individual members of society to learn and to communicate ideas through language. Changes associated with civilization have occurred so rapidly that there has not been enough time for the genetic constitution of human beings to be altered significantly through the process of evolutionary adaptation. Therefore, cultural processes that depend on learning are very important in adapting to new conditions. The following situation illustrates cultural adaptation. As a result of technological advances and economic factors the diet of most people today contains large amounts of refined carbohydrates. One effect of this dietary pattern is the development of dental caries. The cultural response to dental caries has been the development of dental technology. Another cultural adaptation in this situation is the addition of fluoride to water supplies.

Individual Adaptation

On another level, adaptation refers to the many processes by which an individual organism adjusts to conditions in its particular environment.

Inherent Adaptive Responses

There are many *inherent*, or *innate, adaptive mechanisms* by which an organism spontaneously responds to environmental changes. The term adaptation is primarily used in this context in this book. These innate mechanisms may involve ontogenetic (affecting growth and development), physiological, or behavioral responses. Innate adaptive mechanisms are genetically coded and therefore are the products of evolutionary adaptation. They can help the organism cope only with certain types of environmental changes. Sometimes an unusual environmental situation will trigger an innate adaptive response that is inappropriate to the situation.

An example of an ontogenetic adaptive response is the alteration of growth when nutrition is inadequate. A child's growth slows during periods of food shortage. As a result of this mechanism, food energy is conserved. This slowing of growth is accompanied by delayed maturation, so that if the period of deprivation is not prolonged, it is possible to make up most of the loss when adequate nutrition is available again. Many reports indicate that the growth of children was slowed as a result of food shortages in various countries toward the end of the Second World War. Although the growth of children was retarded at that time, the eventual adult size did not differ significantly from the norm for the population.

An example of a physiological adaptive response is tanning of the skin on exposure to sunlight. This mechanism serves to protect underlying tissues by screening out harmful rays of the sun. Physiologically a person adapts to cold by constriction of blood vessels in the skin to reduce heat loss from the body. Those who live in a cold environment for a long time have a higher rate of metabolism to increase heat production. This response is another example of physiological adaptation.

Shivering and moving around are innate behavioral responses to cold. These activities increase heat production by the body. Another example of an inherent adaptive behavior is reflex withdrawal from a noxious stimulus.

Learned Adaptive Responses
In addition to inherent adaptive mechanisms, learned behavioral responses are very important in human adaptation. Thus, for example, in response to cold a person may put on warmer clothing, or light a fire, or adjust the setting of a thermostat in a house. Through learned behaviors, human beings are able not only to adjust to environmental conditions but also to alter the external environment to suit their needs. Learned behavioral mechanisms are particularly important in adapting to psychological and sociocultural factors in the environment.

Psychological adaptation involves intellectual and emotional adjustments to real or imagined environmental conditions as perceived by the individual. Both conscious and unconscious mental processes are used. Psychological adaptation includes the use of defense mechanisms such as rationalization, projection, reaction-formation, dissociation, repression, and substitution. These mechanisms serve the purposes of protecting a person from excessive anxiety and of maintaining self-esteem.

Sensory Adaptation
In *sensory adaptation* the term adaptation is used in a very restricted context to denote the adjustment of sensory receptors to the intensity or quality of stimulation. This adjustment may occur as a heightened sensitivity (e.g., adaptation of the eye to the dark) or as a decreased response to a constant stimulus (e.g., the gradually diminishing sensation of warmth that occurs when a hand is placed in hot water). Sensory adaptation has two aspects, which are complementary. It involves not only a desensitizing process but also a sensitizing process. For example, adaptation to light makes the eyes more sensitive to dark. As a result of sensory adaptation people become aware of changes in the stimuli impinging upon them.

Adaptive Capacity

Human beings are limited in their ability to adapt to environmental changes. Furthermore, not all people have the same capacity to adapt. A person's adaptive capacity is influenced by several factors.

Genetic constitution, or heredity, determines the *adaptive potential* of an organism. The anatomical, physiological, and biochemical characteristics of an individual are genetically determined. Intelligence is also determined, at least partly, by heredity. (The extent to which heredity determines intelligence and the role of environmental influences is controversial.) These characteristics restrict the ways in which a person can respond to changes. The expression of inherited characteristics is modified to varying degrees by environmental conditions, but the limits of development are determined by genetic constitution. For example, heredity determines that a person has two legs. As a result of environmental conditions, however, a person may have one leg amputated in an industrial accident. Subsequently, he or she is not able to regenerate the lost limb: this inability is genetically determined. One can, however, be provided with an artificial leg (cultural adaptation) and can compensate for the loss of a leg by the use of learned behaviors.

Adaptive capacity is influenced by *age*. A person is generally most adaptable during youth and middle life. During infancy and early childhood, and during old age, adaptive capacity is more limited. The repertoire of learned adaptive behaviors of a young child is necessarily limited by lack of experience. Physiological adaptability during infancy and early childhood is restricted because not all the organs and systems are fully developed. In the neonatal period, regulatory mechanisms are not fully developed due to immaturity of the central nervous system. Regulation of fluid balance is more precarious in infancy than in middle life because the infant's immature kidneys are less efficient at concentrating urine. A very young child is more susceptible to infection than an older child or adult because of incomplete development of the immune system.

The exact reasons for the decline of adaptive capacity in old age are not known. The decreased ability of an elderly person to adapt may be due to altered function of the nervous and endocrine systems, which integrate and coordinate adaptive responses. It has also been suggested by Hans Selye that a person is born with a finite amount of "adaptive energy." Adaptive energy is defined as the capacity to perform adaptive work. When a person reaches old age the supply of adaptive energy is almost exhausted. At the moment Selye's theory is just one among many; it has neither been proven nor disproven. In any event, in the early part of life, a person's adaptive capacity is not fully developed. The capacity to adapt develops as a child grows, and it reaches a maximum in adulthood. After that it gradually declines until death.

Anatomical integrity is a factor in adaptability. Loss of body tissue will generally decrease adaptive capacity. The degree to which a lack of anatomical integrity will alter adaptive capacity, however, will depend on the location and extent of the defect. For example, injury to the hypothalamus will seriously impair a person's ability to maintain homeostasis in the face of environmental change because many control centers are located in the hypothalamus. Damage to the cerebral cortex may reduce the ability of a person to adapt psychologically as well as physiologically, but in this case the amount of brain tissue lost becomes more important than the specific area of the loss. Loss of skin (such as may occur with burns) will impair the ability of a person to maintain fluid balance, to regulate body temperature, or to restrict entry of noxious elements from the external environment into the body. Therefore the person will be extremely vulnerable to environmental changes. In this case, the amount of skin lost is critical in determining the ability to survive.

Past experience alters adaptive capacity in that it "sensitizes" a person to a particular environmental situation. Previous exposure to an environmental situation enables one to develop adaptive mechanisms to deal with that particular situation. This process is particularly operative with learned behavioral adaptations, but also occurs when the adaptive mechanism is an innate physiological response. For example, the first time a person is exposed to a particular microorganism he or she may develop an infection. As the body fights the infection, antibodies against the invading microbe are formed. In subsequent encounters with that microorganism the person will be immune to infection because of the presence of these antibodies. The person has developed a protective adaptive mechanism.

Previous exposure is not, however, always helpful in future attempts at adaptation, especially when the adaptive response to the initial experience was inappropriate or unsuccessful. For example, an inappropriate immune response may produce an allergic reaction when the person is subsequently exposed to a particular antigen.

In addition to the effect of previous exposure to environmental situations, past experience in meeting needs also influences adaptive capacity. If a need has not been adequately met in early life, a person's development can be impaired. In addition, that person will have a decreased ability to respond successfully to environmental challenges in later life. For example, inadequate nutrition during the first two years of life can stunt physical growth and interfere with normal development of the central nervous system.

Characteristics of Adaptation

Adaptation is a dynamic process involving the interaction of an organism with the environment in which it lives. The organism forms part of the total environment, and not only does the environment influence the individual organism but the organism also alters the environment. For example, a bacterium secretes toxins into the surrounding medium; a human being cuts down trees to build a house. It has already been pointed out that a constant exchange of substances occurs between an organism and its environment (e.g., exchange of oxygen and carbon dioxide) in order to satisfy basic needs. According to Claude Bernard, the conditions for life are found neither in the organism nor in the environment, but in both at once.

Adaptation is necessary for survival. The more flexible an organism is in its ability to adapt, the greater will be its capacity to survive. For example, if an organism depends on one type of food, it will be able to survive only in an environment that provides that food. If, however, an organism can use a variety of foodstuffs to satisfy its nutritional requirements, it can survive in a much wider range of environments. If a specific food is not available in a particular environment, the organism can adapt by using a different food instead. As already mentioned in the previous section, the capacity to adapt is limited, and varies from one individual to another.

An organism can adapt more readily to a gradual change in environmental conditions than to a rapid change. In other words, if the body has sufficient time it can adapt to a greater challenge than if it has to adapt quickly. For example, if a blood vessel serving a particular tissue is gradually blocked by a slowly developing process, an alternate blood supply (collateral circulation) to that tissue can develop. When the major blood supply is finally cut off, the tissue is not seriously damaged. When a blood vessel is suddenly blocked, however, the tissue may be damaged as a result of inadequate blood flow because a collateral circulation has not been developed.

Also, if a person is exposed to an environmental situation for a prolonged period of time, that person will gradually achieve a more satisfactory degree of adaptation. For example, if one is exposed to a low partial pressure of oxygen such as occurs at high altitudes, the immediate adaptive response is an increased rate of pulmonary ventilation and increased pulse rate. In spite of this mechanism the person may suffer impaired mental functioning and decreased capacity for muscular work. If the person remains at high altitude for several days, or weeks, or years, he or she gradually becomes better adapted. The low oxygen tension has fewer adverse effects on the body and the person is able to work harder. This increased tolerance to low oxygen tension occurs because the body develops additional adaptive mechanisms: increased production of erythrocytes and hemoglobin; increased blood volume; increased number of capillaries to hypoxic tissues; increased diffusing capacity for oxygen through the pulmonary membrane.

Adaptation requires energy and an organism tends to use adaptive mechanisms that are most economical of energy. It takes less energy to use an old adaptive mechanism than to develop a new one. Therefore, a person usually uses a previously developed technique when confronted with a new situation. The old method may or may not be appropriate or successful in the new situation.

Adaptation involves adjustment to the total environmental situation. An organism does not necessarily respond to one environmental factor in isolation. For example, at high altitude a person must simultaneously adapt to hypoxia and to cold. The response to cold in this situation may be different from the response to cold when oxygen is adequate. One response to cold is to increase activity to produce more heat. But this activity increases the oxygen requirement and so may be impracticable for survival under conditions of hypoxia.

Adaptive responses are not the same for every individual. The nature of an adaptive response depends not only on the evoking stimulus, but also on the internal state of the organism at the time the stimulus is received. The response also depends on the way the individual *perceives* the stimulus, and the *meaning* the stimulus has for that individual. Also, the range of adaptive responses is limited by genetic constitution, and no two people (with the exception of identical twins) are genetically alike. For these reasons, different people may adapt differently in the same situation.

An organism maintains its identity in spite of the use of adaptive mechanisms. Although a person makes adjustments in response to environmental changes, she or he maintains a stability of form and function and a general pattern of behavior that characterizes that person as a unique individual.

Adaptive mechanisms are attempts to maintain homeostasis and preserve the integrity of the organism. Some adaptive responses are elicited by conditions in the external environment. In other cases the stimulus for an adaptive response arises from within the organism as a result of an unsatisfied need.

Homeostasis and adaptation are complementary concepts. For optimum functioning of the body, the internal environment must be kept constant within narrowly defined limits. In other words, a person must maintain homeostasis. In order to maintain homeostasis a person must constantly make rapid adjustments to changes in the environment. That is, she or he must adapt. Ideally, adaptive responses are such that they enable a person to function satisfactorily under the changed conditions.

HOMEOSTATIC MECHANISMS

The body has numerous homeostatic control mechanisms. These mechanisms operate continuously in order to minimize the effects of disturbances and preserve a stable internal environment. In some cases, homeostatic regulation consists of storage of materials when there is excess (e.g., glucose converted to glycogen) and their subsequent release in times of need (e.g., glycogen reconverted to glucose). If the excess cannot all be stored, it may be eliminated from the body. In other cases, homeostatic regulation involves altering the rate of various processes (e.g., altering heat production to maintain constant body temperature). The circulation of the blood is critical in maintaining homeostasis because it is necessary for the distribution of substances (and also heat) throughout the internal environment. Therefore a number of mechanisms exist to maintain blood pressure at the desired level and assure continuous flow of blood through the tissues. All these regulatory mechanisms are controlled by the autonomic nervous system and the endocrine system.

The maintenance of homeostasis requires that any tendency toward change is automatically met by increased effectiveness of the factors that resist the change. This task is accomplished by homeostatic mechanisms operating according to the principle of *negative feedback control.*

In a feedback control system the consequences (output) of an action produced in a system are in some way returned or *fed back* to influence the causes (input) of the action. The concept of a system, as used in this context, refers to a set of components that act together and that can be treated as a whole. The stimuli or disturbances that act on the system are called inputs. The consequence of these inputs is the output or response. In a feedback system, the feedback may be negative or positive. With negative feedback, if the system is disturbed, the disturbance (input) triggers a series of events that counteract the disturbance and restore the system to its original (or desired) state. Negative feedback control mechanisms are therefore negative to any attempt to change the system and they favor stability. Negative feedback control is very common in living organisms. Positive feedback is positive to change. With a positive feedback mechanism, a disturbance to the system