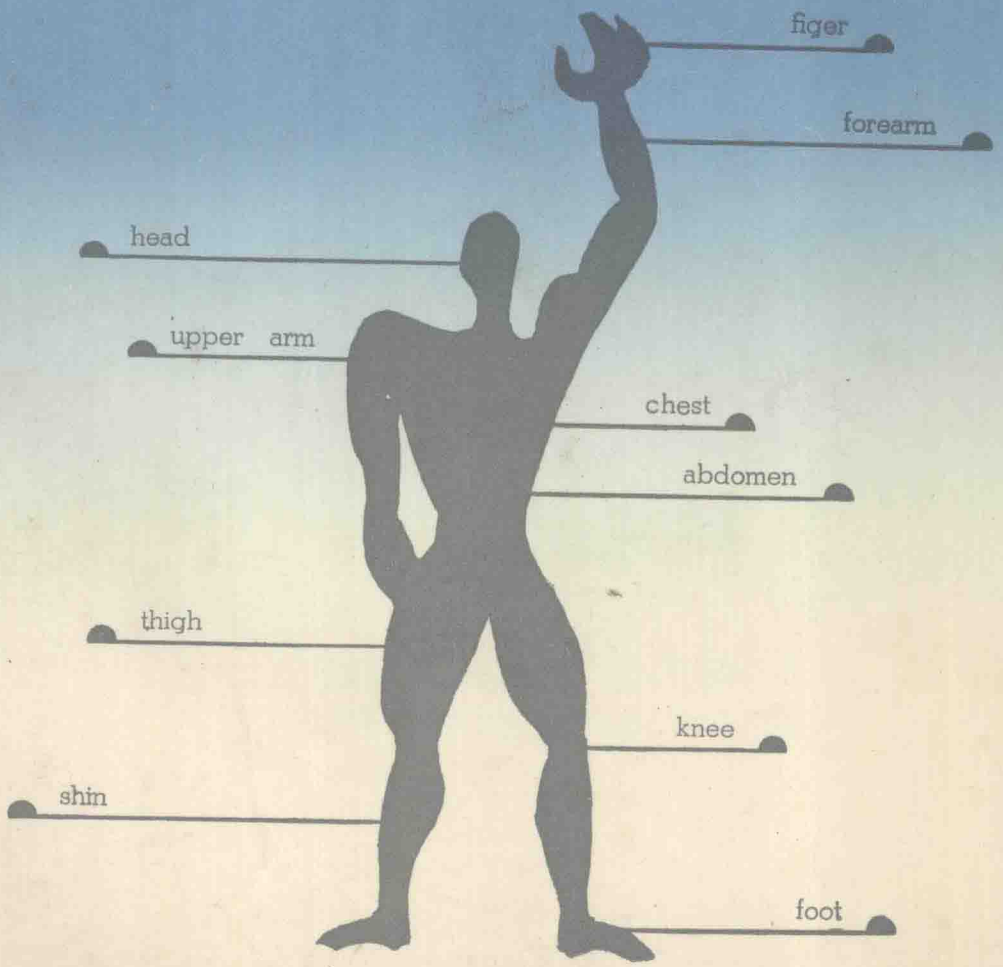
HUMAN PHYSIOLOGY

HAN JISHENG
Editor-in-Chief



SHANGHAI SCIENTIFIC & TECHNICAL PUBLISHERS

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Editor-in-Chief: **HAN Jisheng**
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PREFACE

Physiology, just like anatomy, has long been regarded as one of the main courses in basic medical sciences for the medical students. It deals with the basic knowledge and ideas that are indispensable to a physician in his medical practice. As English has become a universal language in science and technology, it is apparent that if a student in medicine can learn physiology in both Chinese and English, it would be an invaluable benefit for his (her) future carreer as a physician or research scientist, and to keep up with the rapid advance in biomedical sciences. In fact this has been the personal experience for many outstanding professors and physicians who have made magnificiant contributions in China today. It was on the basis of this understanding that we decided three years ago to use English technical terms in our teaching of the medical students. To facilitate this approach, we have published a notebook of HUMAN PHYSIOLOGY in English, which has been well received by the students in Beijing Medical University. To cope with the "reform and open policy" today, we decided to rewrite the book to meet the requirement of medical students in 1990's. Aside from authors in the Beijing Medical University, new authors have been recruited from Shanghai Medical University, Dalian Medical College and the Norman Bethune University of Medical Sciences. All of them are the experts in the field where they have been teaching and engaged in research for decades.

As a teacher in Physiology and editor of a couple of biomedical journals, I fully realize that it is by no means an easy task for us Chinese professors to write a textbook in English, that is scientifically meritorious and literarily readable. We were, however, very fortunate to have Dr. Tang Peichin, an American Professor of Physiology of Chinese descent to help us in this regard. He was very kind to read all chapters and touch up every page of the draft very carefully in a relatively short period of time. I would also like to express my sincere thanks to Professor Yu Yingxin who spent a great deal of her valuable time in making arrangements with the authors and the Publishers, and in making the list of vocabularies in collaboration with young colleagues Xia Yu, Wang Jianping, Mo Li, and others.

As mentioned above, this book is a revised edition of the "HUMAN PHYSIOLOGY" published four years ago. The unique contribution made by Professor Fan Shaoguang in organizing that edition is heartedly acknowledged. We are also indebt to the staffs

of the Shanghai Scientific and Technical Publishers for their efficient handling of the printing and for their efforts in publishing the book in a period of one year.

I would confess that although all the authors have had experience in teaching Physiology in English for at least 2–3 years, and we have made every endeavour to make this project a success, the publishing of this book should still be regarded as a trial run in China. We are looking forward to having comments and suggestions from colleagues and students who have used this book. This would certainly help us to improve our book in the next edition, thereby enable us to provide a better service to our readers.

Han Jisheng
Professor & Chairman
Department of Physiology
Beijing Medical University
April, 1989

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INTRODUCTION

PHYSIOLOGY: DEFINITION AND METHODOLOGY

PHYSIOLOGY AND RELATED SCIENCES

Physiology is one of the biological sciences which deals with the phenomena exhibited by living organisms. It is a study of the normal functions of organs and organ systems of the body, the conditions under which these functions are carried out and the me chanisms by which they are achieved.

Besides physiology, the basic medical sciences include biology, embryology, genetics, anatomy, histology, biochemistry, biophysics, pathophysiology, pathology, microbiology, immunology, etc. Although taught separately as different courses, these branches of basic medical sciences are closely inter-related and inseparable, forming a solid scientific basis for practice of medicine.

METHODOLOGY

In the early days knowledge of the functions of the body was acquired through observations of human and animal activities. Starting from the seventeenth century the

passive method of observation was gradually replaced by the active method of planned experimentation, using monkeys, dogs, cats, rabbits, rats, mice, frogs, and other forms of living organisms. Experiments may be *in vivo*, performed on the whole animal, or *in vitro*, performed on isolated tissue or organ. *In vivo* study, acute experiments may be performed on animals under anesthesia or with transected brain, and chronic experiments on conscious animals for a long period of time.

There is no doubt that the knowledge gained in animal experiments is indispensable for the understanding of life activities in humans. However, owing to the species difference, the application of results obtained in animals, especially in lower animals to human beings should be made with caution. Moreover, results obtained in anesthetized animals may be qualitatively different from that obtained in conscious animals. Thanks to the drastic advances in science and technology in the recent decades, many experiments can now be performed in intact conscious animals or even in humans, without the complication of anesthesia or surgical operations. Advance in technology also made it possible to perform sophisticated *in vitro* experiments to gain a deeper insight into the mechanisms of life activities at the cellular and molecular levels. As a result, there is a tendency of using less and less acute experiments, and this trend is likely to continue in the years to come.

FUNDAMENTAL CHARACTERISTICS OF LIVING ORGANISM

METABOLISM

All vital processes of the body involve myriad chemical reactions which collectively constitute the metabolism. It includes all the material and energy changes that occur in the body, and in its broadest sense is identical with the term "life". All the changes fall into two categories: catabolic and anabolic reactions. Catabolic reactions involve the breakdown of larger, more complex molecules into smaller, simpler molecules, during which energy is released for the activity of the body. Anabolic reactions involve the synthesis of complex molecules from simpler ones. Anabolism and catabolism are two opposing activities taking place simultaneously in the cell. Because of various kinds of enzymes the chemical reactions are processed smoothly and rapidly under very mild conditions, such as in the temperature range of less than 40℃ and in an almost neutral acidity of the body fluid.

It is apparent from the above discussions that material and energy metabolism are two intimately related aspects of one and the same process. It is for the sake of convenience in teaching that energy metabolism is discussed in physiology, and material metabolism in biochemistry.

EXCITABILITY

Changes in the external or internal environment can induce changes in the activity of a living organism, or, in physiological terms, environmental stimuli can elicit response of the tissues of the body. Among the common environmental changes or stimuli are mechanical, thermal, chemical, electric, photic, phonic, etc. Response can be classified into two types: excitatory response or excitation, and inhibitory response or inhibition. Excitation signifies an increase in activity, such as contraction of a muscle, acceleration of the heart beat or secretion of tears. Inhibition, on the contrary, is a decrease in activity, such as the slowing of the heart beat (as a result of the activation of the vagus nerve). The property of living organisms that permits them to react to stimuli is defined as excitability. This is a fundamental property common to all tissues and cells.

What then is the objective manifestation of the excitation common to all tissues? An adequate stimulus applied to excitable tissue such as muscle, nerve or gland can induce an electric change spreading along the muscle, nerve or gland, that is called "action potential". Action potential appears simultaneously with the conduction of excitation along the nerve fiber, and always preceeds the contraction of a muscle, thereby is regarded as an indication of excitation.

The excitability of a tissue can be assessed by measuring the intensity of a stimulus that is needed for eliciting a minimal reaction or an action potential in an excitable tissue. The higher the intensity of stimulus needed (the threshold of stimulus), the lower the excitability, and vice versa.

A stimulus is defined not only by its intensity, but also by the time period used by the stimulus. A weaker stimulus needs a correspondingly longer time to be effective. However, below an absolute threshold intensity, the rheobase, excitation never ensues no matter how long the stimulus is applied. The utilization time needed at a stimulus intensity twice the rheobase is called chronaxie, and this is commonly used as a measure of a tissue's excitability. Several modifications have been introduced to provide a more precise index of excitability in various tissues.

REPRODUCTION

A process by which an animal produces one or more individuals similar to itself is called reproduction or self-reprication. The individual can survive without reproduction, but the species can not.

INTEGRATION AND REGULATION OF BODY FUNCTIONS

HOMEOSTASIS

A living organism is constantly interacting with its surrounding environment, there-

fore the organism and the environment should be viewed and studied as a whole. In contrast to the vigorously changing external environment to which the body is being exposed, the cells of the body are living in an environment formed by the interstitial fluid which has been termed the "internal environment". Since normal cell function depends upon the constancy of this environment, it is not surprising that in higher animals an immense number of regulatory mechansims has evolved to maintain the "nearly constant condition of the internal environment", for which W. B. Cannon coined the term "homeostasis". In fact, a large part of physiology is concerned with the regulatory mechanisms that act to maintain the dynamic equilibrium for the physical and chemical constancy of the internal environment.

REGULATION OF BODILY FUNCTIONS

Nervous Regulation. The nervous system may be regarded as the main coordinator of the activities of the body, and the main form of activity of the nervous system is reflex. Under the mediation of the nervous system, a particular stimulus elicits a particular response. For example, burning of the finger tip elicits withdrawal of the hand; acid in the mouth elicits secretion of large amount of saliva. The anatomical basis of reflex activity is the reflex arc which has three basic components: an afferent limb conveying signals from periphery to the central part of the nervous system, an efferent limb carrying signals from the central nervous system to the effectors (such as skeletal muscles, secretory glands, etc), and the reflex center located within the central nervous system.

As mentioned above, most of the basic reflex activities are stereotyped. However, the fixed relation between stimulus and response in some basic reflexes does not exclude the possibility of their being modified by experience. In fact many reflexes in the adult individual are not congenitally available, but are learned by the individual through life experience. For example, withdrawal of the hand may occur in response to the viewing of a fire without being actually burned; saliva may be secreted in response to seeing a fruit without actual tasting of it. These reflexes are categorized as conditioned reflexes to be differentiated from un-conditioned reflex which is congenitally possessed and stereotyped in nature.

Humoral or Neuro-humoral Regulation. Humor means fluid, or in a specific sense, body fluid including blood, lymph, interstitial fluid, etc. Metabolic products or special chemicals produced by certain tissue are carried by body fluid to act upon other tissues located at a distance from the original one. Hormones or endocrines are the main humoral factors playing a regulatory role on the body function. Some endocrine systems act independently of the nervous system. However, in many cases the endocrine system is so closely related to the nervous system that it can be regarded as an extension of the efferent limb of the reflex arc. In this instance it is

called neuro-humoral regulation.

Compared with the nervous regulation which is characterized by rapidity and accuracy in response, humoral regulation is, generally speaking, slow in onset, diffuse in nature, and often longer in duration.

Auto-regulation. In certain cases a tissue or organ can respond directly to the environmental change, depending neither on nervous nor on humoral control. For example, distension of the cardiac chamber by surplus amount of venous blood return results in an increase in the contractile force of the cardiac muscle, thus ensuring the complete emptying of the ventricle. This form of regulation is called auto-regulation, forming a supplementary mechanism to the major control systems.

FEEDBACK CONTROL OF THE BODY FUNCTION

In physiology there are two closely related terms with similar but not identical meanings: control versus regulation. Regulation implies more than control, because it signifies those controls that tend to preserve a relatively constant condition. For example, the action of the heart is controled by sympathetic and vagus nerves, but blood pressure is regulated by various control systems to keep it at an almost constant level.

Usually, a constancy of physiological variable requires a feedback mechanism that feeds the output information back to the control system so as to modify the nature of the control. Feedback mechanisms consist of two forms: negative and positive feedbacks (Fig. 1-1). Negative feedback signals always produces an effect opposite to that produced by the initiating stimulus. When the output of the control system becomes excessive, a detector would send back signals to suppress the control system so as to

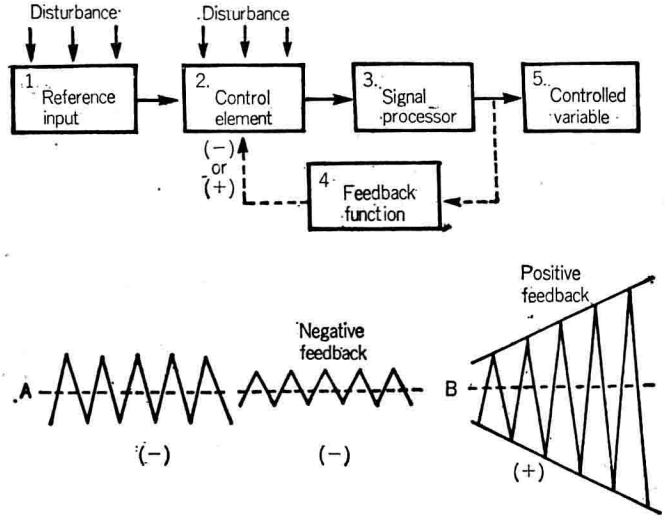

Fig. 1-1 Negative and positive feedback systems

return the variable toward a previously set level or the mean physiological value, thus maintaining homeostasis.

In contrast to the negative feedback mechanism which restrains the activity of the control system, a positive feedack circuit intensifies the activity of the control system. For example, starting of urination results in a continuous and even stronger contraction of the urinary bladder to ensure its complete emptying. While positive feedback is rarely seen in physiological conditions, it often happens in pathological conditions, resulting in a vicious cycle causing serious damage to the organism.

Han Jisheng

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CHAPTER 2

THE CELL AND ITS FUNCTION

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THE CELL

The basic living unit of the body is the cell and each organ is actually an aggregate of many different cells held together by intercellular supporting structures. Each type of cell is specially adapted to perform one particular function. However much the many cells of the body may differ from each other, all of them have certain basic characteristics that are alike. All cells use oxygen which combines with carbohydrates, fat, or protein to release the energy essential to the maintenance of life. They all deliver their metabolic end-products into the surrounding fluids. Almost all cells also have the ability to reproduce.

ORGANIZATION OF THE CELL

The two major parts of a cell are the nucleus and the cytoplasm. The nucleus is separated from the cytoplasm by a nuclear membrane and the cytoplasm from the surrounding fluids by a cell membrane. The different substances that make up the cell are collectively called protoplasm which is composed mainly of five basic substances: water, electrolytes, proteins, lipids, and carbohydrates. Of particular importance are the nucleoproteins, present both in the nucleus and in the cytoplasm. The nucleoproteins of the nucleus contain deoxyribonucleic acid (DNA) which constitutes the genes that control the overall functions of the cell as well as the transmission of hereditary characteristics from cell to cell.

The cell is not merely a bag of fluid, enzymes, and chemicals. It also contains highly organized structures called organelles. Some principal organelles are the cell membrane, nuclear membrane, endoplasmic reticulum, mitochondria, lysosomes, Golgi complex, centrioles, cilia and microtubules.

THE CELL MEMBRANE

The cell membrane which completely envelops the cell is a very thin elastic structure only 7.5 to 10 nanometers thick. Its approximate composition is proteins, 55%; phospholipids, 25%; cholesterol, 13%; other lipids, 4%; and carbohydrates, 3%. It serves as a permeability barrier that allows the cell to maintain the composition of the

cytoplasm which is far different from that of the extracellular fluid. The intracellular fluid contains large amount of potassium, magnesium, and phosphate ions instead of the sodium and chloride ions found in the extracellular fluid.

MEMBRANE STRUCTURE

The basic structure of the cell membrane is a lipid bilayer. A phospholipid molecule has a polar hydrophilic (water soluble) phosphate head group and two extremely nonpolar hydrophobic (fat soluble) fatty acyl chains. In an aqueous environment, it is energetically most stable for the phospholipids to form structures that allow the fatty acyl chains to be hidden from water. One of such structures is the lipid bilayer (Fig. 2-1).

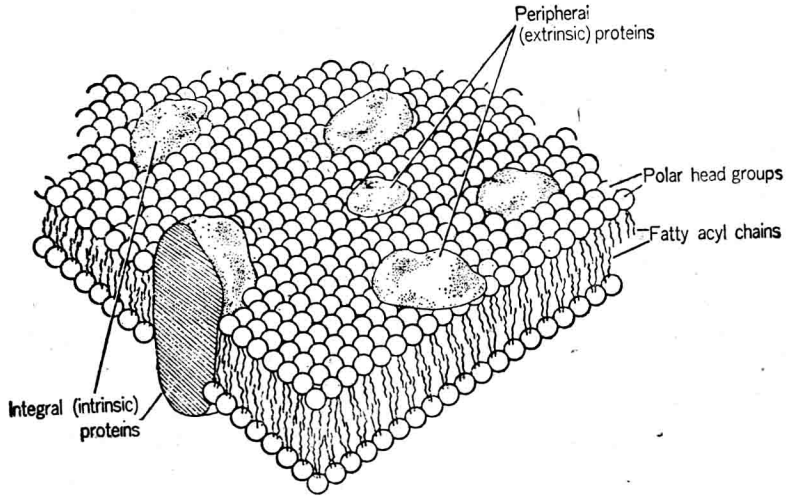

Fig. 2-1 Schematic representation of the fluid mosaic model of membrane structure showing integral proteins embedded in the lipid bilayer matrix of the membrane and peripheral proteins associated with the polar head groups.

There are two types of membrane proteins: the integral proteins that protrude all the way through the cell and the peripheral or extrinsic proteins that are attached only to the surface of the membrane (Fig. 2-1). The integral proteins usually have water-soluble portions on both ends and fat-soluble portions in the middle. It is the fat-soluble portion that dissolves in the lipid bilayer while the water-soluble portions protrude to the outside and inside of the membrane. The integral proteins provide structural pathways through which water and water soluble substances, especially the ions, can diffuse between extra- and intra-cellular fluids. However, these proteins have selective properties that cause preferential diffusion of some substances more than others. Some of them can also act as enzymes. The peripheral proteins interact with the membrane lipids predominantly by charge interactions with the water-souble polar head groups. They are either entirely or almost entirely on the inside of the membrane

and normally attached to one of the integral proteins. These peripheral proteins usually function as enzymes.

The membrane carbohydrates are the "glyco" portion of the protruding glycoprotein molecules and usually located on the outside of the membrane. They play a major role in immune reactions and often act as receptors for binding hormones. Cell membranes are fluid structures and most lipid and protein molecules are free to move in the bilayer plane.

MEMBRANE TRANSPORT

Different substances are transported through the cell membrane by different processes.

Simple Diffusion. Substances that are soluble in lipids such as oxygen, carbon dioxide, alcohol, etc. can dissolve in the cell membrane and diffuse across it.

Facilitated Diffusion. Some substances which are insoluble in lipids, such as Na^+, K^+, glucose, amino acids, and water pass through the cell membrane by facilitated diffusion. There are two types of facilitated diffusion.

(1) Carrier mediated diffusion. Substance combines with a carrier to form a compound substance that is soluble in the lipid so that it can diffuse through the membrane. The carrier itself is probably a small protein or lipoprotein.

(2) Channel mediated diffusion. Ions cross membranes via ion channels. The ease with which ions pass through some of these channels is controlled (gated) by voltage or by agents such as neurotransmitters.

Active Transport. Molecules or ions of some substances (such as Na^+, K^+, I^-, Ca^{2+}, etc.) are transported through a cell membrane from a dilute solution to a concentrated solution. This process of moving molecules uphill against a concentration gradient is often called a "pump," such as sodium–potassium pump, iodine pump, etc. The sodium–potassium pump is a unique protein in the cell membrane (Na^+ –K^+ activated ATPase). Energy must be expended to maintain the pumping action.

Exocytosis and Endocytosis. Particles that are secreted by cells move from the endoplasmic reticulum to the Golgi complex, where they are packaged into secretory granules. These membrane–bound granules move along tracks of microtubules to the cell membrane. The granule membrane and the cell membrane then fuse, and the area of fusion breaks down, leaving the contents of the granule outside the cell and the cell membrane intact. This process is called exocytosis. It requires Ca^{2+} and energy, but the detail mechanisms responsible for the breakdown of the membrane are unknown.

Endocytosis is the reverse of exocytosis. One form of endocytosis, called phagocytosis ("cell eating"), is the process by which bacteria, dead tissue, or other bits of material visible under the microscope are engulfed by cells such as the polymor-

phonuclear leukocytes of the blood. The material makes contact with the cell membrane, which then invaginates. The invagination is pinched off, leaving the engulfed material in the membrane-enclosed vacuole and the cell membrane intact. Pinocytosis ("cell drinking") is essentially the same process, the only difference being that the substances ingested are in solution and hence not visible by the microscope.

MEMBRANE RECEPTORS

Neurotransmitters and nitrogen-containing hormones react with receptors on the external surface of the membrane of their target cells. The application of genetic engineering techniques has unraveled the primary structure of many receptor proteins, such as the receptors for acetylcholine, 5-hydroxytryptamine, substance P, etc.

The binding of hormone or neurotransmitter with the receptor activates a series of post-receptor events. For example, activation of the enzyme adenyl cyclase causes immediate conversion of cytoplasmic ATP into cyclic AMP. which mediates their physiologic effects. Cyclic AMP (cAMP) is frequently called the "second messenger" (the "first messenger" being the original stimulating neurotransmitter or hormone). Fig 2-2 illustrates the function of the cyclic AMP mechanism in more detail. The types of effects that will occur inside the cell are determined by the character of the cell itself. There are other second messengers, such as cyclic guanosine monophosphate (cGMP) and Ca^{2+}. cGMP usually promotes intracellular reactions that are different from those promoted by cAMP. Many intracellular effects of Ca^{2+} are mediated via a ubiquitous calcium binding protein called calmodulin. Calmodulin is an acidic peptide with four

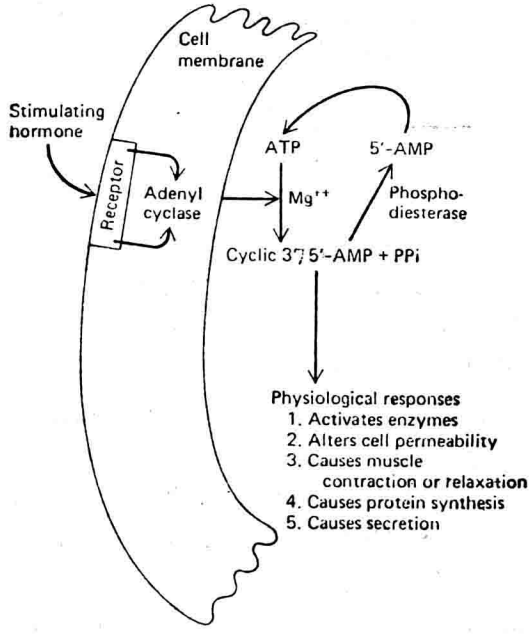

Fig. 2-2 The cyclic AMP mechanism by which many hormone exert their control of cell function.