



普通高等教育“十一五”国家级规划教材

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## 医学英文原版改编双语教材

(供临床、基础、预防、口腔、药学、检验、护理等专业使用)

### TEXTBOOK OF PATHOPHYSIOLOGY

# 病理生理学

Original Editors

Stephen J. McPhee  
Vishwanath R. Lingappa  
William F. Ganong

Chief Editors of Adaptation Edition

Wang Jianzhi (王建枝)  
Chen Guoqiang (陈国强)



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# Preface for Adaptation Edition

Wang Jianzhi & Chen Guoqiang

Pathophysiology is an important subject bridging basic and clinical medicine. According to the Program in Adapting English Textbook Series in Medicine, we tried to recompose this textbook based on the prototypic book termed "Pathophysiology of Disease", with the informed consent. The excellent original book, which was edited by Stephen J. McPhee, Vishwanath R. Lingappa and William F. Ganong and published by McGraw-Hill, included 25 chapters developed chiefly by organ system, and each chapter was divided into sections emphasizing anatomy, physiology, pathology, disordered physiology, common clinical presentations, and mechanisms underlying symptoms and signs.

To accommodate to the current teaching peculiarity of pathophysiology in China, we could only select limited chapters, i.e., "blood disorders", "nervous system disorders", "pulmonary disease", "cardiovascular disorders", "liver disease", "renal disease" from the original book. Therefore, we added new chapters to the recomposed book. In each chapter, more emphasis is given on the disease mechanisms and the alterations in function and metabolism, and the contents directed to anatomy and pathology are mostly eliminated. In addition, we also changed the chapter title of "coagulation and anticoagulation imbalance" into "disturbance of hemostasis" by referring to the most recent edition of the Hill's Internal Medicine.

The new book is composed of 19 chapters that are organized by three major portions. The first portion mainly focuses on the fundamental concepts and major basic pathological processes, including "conspectus of disease", "Water and electrolytes balance and imbalances", "acid-base balance and imbalance", "stress", "fever", "ischemia-reperfusion injury", "shock", and "hypoxia". Knowledge of these basic pathological processes is essential for understanding the mechanisms of diseases. The second portion, which includes signal transduction, cell proliferation/differentiation/apoptosis and the related diseases, deals with cellular and molecular mechanisms in diseases. The last portion of the book directs to pathophysiology of organs, which covers blood, heart, lung, liver, kidney, brain, multiple organ dysfunction and metabolic syndrome. As this part of the original book matches up to our teaching system, we are encouraged to make maximal use of the contents from the prototype of the book. The orientation for each chapter is organized as sections emphasizing the general concepts, physiology (in some chapters to retain the style of the original book), etiology and pathogenesis, the alterations of metabolism and function, as well as principles for prevention and therapies. Additionally, we also added a new chapter namely "metabolic syndrome" according to the most recent attention to this disorder.

The intended readers of this book are medical students, including undergraduates and post-graduates, in their basic pathophysiology courses. We hope that these students will find this book useful for their understanding how pathological agents cause various disease states. We also expect that physicians-in-training and physicians will find the book helpful



in comprehending how and why various disease states appear. The clinical doctors may find the book useful as a refresher that updates their understanding of the disease mechanisms. Nurses and other medical practitioners may find that the concise format and broad/new scope of the book facilitate their understanding of the basic disease entities.

We are most grateful to all the contributors for their hard and efficient work to make this book available in a limited time period. We greatly appreciate Prof. Wang Dixun for his guidance and Dr. Wang Xiaochuan for his aspiring secretary work. We would also like to thank Drs. Yang Ying, Tian Qing and Fang Zhengyu for their full support in final proofreading and formatting of the book.

Because of the limitation of words, we can not provide all references. So, we feel apologized for their deletions. We also would like the readers to point out the errors or offer comments or suggestions. Such feedback will be very helpful for us to revise this book into a better version in the future.

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# Chapter 1 Conspectus of Disease

Wang Jianzhi

In this chapter, we will discuss from a general view the concept, etiology, pathogenesis and outcome of disease.

## CONCEPT OF DISEASE

Disease is referred as aberrant manifestation of deregulated homeostasis caused by harmful agents. The development of a disease is definitely a pathologic process with a characteristic set of signs and symptoms involved in the whole body or any of its parts. For instance, pituitary diseases are disorders of the anterior or posterior pituitary gland which usually manifest as hypersecretion or hyposecretion of pituitary hormones. Pituitary mass lesions may also compress or affect the optic chiasma and other adjacent structures and thus cause relevant disorders.

Disease reflects an opposite situation of health. Health used to be defined as the state of the organism when it functions optimally without evidence of disease. Recently, the definition of health from World Health Organization (WHO) emphasizes that health indicates not only without any evidence of disease, but also a state of complete well-being physically, mentally and socially.

Additionally, there is a situation, in which the person does not show specific symptoms and signs of disease, but lives a low-quality of life both physically and mentally; this is called "sub-health".

Another concept needs to emphasize here is "basic pathological process", which indicates some common and collective pathological alterations presented in a group of diseases. For example, inflammation is a basic pathological process for various infectious diseases, such as arthritis, pneumonia, *etc.*, and so does for hypoxia, stress, edema, acidosis, and so on.

For some diseases, the etiology, pathology, pathogenesis and prognosis are still unknown at present. Therefore, scientific research aimed to explore the mechanism of diseases and thus to develop effective

cures for the diseases is always an obligatory duty for our medical scientists.

## ETIOLOGY OF DISEASE

Etiologic factors involved in diseases include causative, predisposing and precipitating factors, which contributes to the onset of diseases.

## CAUSES OF DISEASES

Among different causes, a wide range of extrinsic and intrinsic factors are described as follows.

### Extrinsic Causes

The extrinsic causes include: ① Biological agents: Biological agents are usually referred as microorganisms and parasites, such as bacteria, virus, fungi, rickettsia, spirochete, *etc.*. Certain bacteria produce exotoxins that interfere with cellular production of ATP; and others such as Gram-negative bacilli release endotoxins that cause profound cell and blood vessel changes. Viruses enter the cells and disrupt the intracellular homeostasis. Still other microorganisms produce their effects via inflammatory or immune mechanisms; ② Chemical agents: Numerous chemical agents can damage cells by various pathways. For instance, corrosive chemicals, such as strong acids and alkalis, can destroy cells at the site of contact. Other chemicals are selective in their sites of action, such as binding of carbon monoxide to hemoglobin; ③ Physical agents: Physical agents include mechanical injuries, extremes of temperature, electricity and radiation. Different from chemical or biological agents, most of the physical factors only participate in the initiation but not in the development of the diseases. Generally, the injuries caused by physical factors are nonspecific, but the degree of vulnerability can be different. For instance, all cells are susceptible to ionizing radiation, but the rapidly proliferating cells of the bone

marrow and the gastrointestinal epithelium are more susceptible than other cells; ④ Nutritional imbalance: Nutrients from the external environment are necessary because they provide the materials for growth and maintenance of body constituents. Either excesses or deficiencies of nutrients predispose cells to injury. For example, high lipids and carbohydrates diet predispose a person to obese disease, atherosclerosis and diabetes. The most common nutritional deficiency is the lack in certain constituents, such as vitamins, calcium, and trace elements. Iron deficiency anemia, scurvy, beriberi, and pellagra are examples of deficits in specific vitamins or minerals. Oxygen is vital to normal cellular metabolism. Therefore, oxygen must be constantly and adequately supplied to the cells. If the oxygen supply is insufficient or interrupted, it will lead to cell injury.

### Intrinsic Causes

The major intrinsic causes are: ① Genetic factors: Genetic aberrancies may be caused by single or polygenic mutations. Genetic disorders are apparent at birth or shortly thereafter, and they are transmitted by defective genes, such as sickle cell anemia, and colorblindness; ② Congenital factors: The disorders are of a developmental nature and most of them are nongenetic. For example, congenital birth defects, mental or physical, may be due to a developmental error during pregnancy. The fetus is usually susceptible to not only infectious diseases but also diet and drug-taking of the mother during intrauterine life; ③ Immunological factors: Although the immune response is a normal protective mechanism, it may cause diseases when the response is deficient (immunodeficiency disease), or inappropriately strong (allergy or hypersensitivity), or misdirected (autoimmune disease); ④ Psychological factors: Anxiety, strong or persistent psychological stimulation or stress may lead to mental illness and may be related to some diseases, such as hypertension, peptic ulcer, coronary heart disease, and depression.

Whether or not a person exposed to harmful attacks become ill is influenced not only by the above-mentioned causative agents, but also by precipitating and predisposing factors. When the cause is extremely potent, the precipitating and predisposing factors will be not or less significant in determining the onset of illness.

## PREDISPOSING FACTORS

A predisposing factor refers to the factor that influences the susceptibility or resistance to certain disease. It includes the genetic constitution, physiological make up, as well as various psychological characteristics of the organisms.

### Genetic Constitution

It is generally recognized that the sum of the genetic and environmental constituents makes a person more or less likely to develop diseases. Some diseases show significant genetic intentions and the most striking evidence in this is the finding that 90% of ankylosing spondylitis patients possesses human leukocyte antigens (HLA) B27.

### Physiological Diathesis

The structural states and functions of body systems adjust the resistance to illness. Every organism has a surface membrane that forms a barrier between the internal and external environments. Disruption of the surface membrane will provide a pathway for noxious elements to enter the body. Additionally, the body has many protective reflexes that maintain the homeostasis in response to various stimuli.

### Psychological Characteristics

To a same illness, some people do not suffer as much as the others simply because they have a more optimistic attitude to life. Psychological defenses may also prevent a stressful irritant from causing a pathological response.

## PRECIPITATING FACTORS

The function of these factors is to intensify the effects of causative factors and promote the onset and development of diseases.

### Natural Conditions

Weather condition and geographical environment may influence the onset of illness. For example, the development of some epidemical diseases is closely related with the geographical environment in which these diseases are easier to occur and to spread.

## Physical Condition

A person may be predisposed to some diseases if he is in a status of physical or mental fatigue or anxiety. And a person may be more vulnerable to myocardial infarction if he has hypertension. A person is most apt to develop a cold if he has been exposed to cold environment.

## Social Condition

Poor labor and hygiene conditions are apt to induce certain occupational and infectious diseases. Social environment involves a significant change in a person's mood and life style. Mood changes can bring about physiological changes mediated by the central nervous system. Any of these factors is in itself not usually sufficient to cause disease, but could influence the frequency or severity of illness.

In summary, specific causes and predisposing factors together determines the disease occurrence, and the precipitating factors influence the onset and development of illness. It is important to recognize that most of the diseases do not have a single cause. Rather, many diseases are multifactorial in origin. This is particularly true in hypertension, atherosclerosis and diabetes, namely "metabolic syndrome".

## PATHOGENESIS OF DISEASE

Pathogenesis of disease refers to the rules and mechanisms underlying the development or evolution of the diseases. It studies how the primary pathological agents cause disease in organism and how the disease develops. Diseases may happen through daedal mechanisms and most of them are still not fully understood, here we just discuss some mechanisms in common sense.

## GENERAL RULES FOR PATHOGENESIS OF DISEASES

The general aspects for a disease to take place and to develop include the disruption of homeostasis by pathological insults, the body's response to damages and anti-damage activities, the reversal role of cause-consequence in the disease process, and the comprehensive mutual-interactions between systemic and local regulation.

## Disruption of Homeostasis

The term of homeostasis denotes the process whereby the internal environment of an organism tends to remain balanced and stable, which is required for optimum functioning. Disruption of homeostasis by harmful agents may cause diseases.

## Process of Damage and Anti-damage

Damages are usually made when a variety of harmful insults attack the body. During this process, anti-damage responses are also induced in the body to restore the normal situation. For instance, when tissue becomes infected (damaged), blood stream to the injured region will be increased accordingly to remove harmful substances and cellular debris, or to produce antibodies against further invading organisms that cause infection (anti-damage). Therefore, the onset and development of a disease depend on the strength of damage and anti-damage factors. It is to emphasize that there is no critical borderline between damage and anti-damage processes and overdo of anti-damage process will cause new injury to the body. For example, in early stage of a burning injury, constriction of small blood vessels is useful for maintaining proper blood pressure. However, sustained vasoconstriction will aggravate hypoxia, and leads to massive cellular necrosis and dysfunction.

## Alternation of Cause and Effect

Rule of alternate cause-effect is always seen in the onset and development of diseases. For example, the bone marrow produces more erythrocytes to provide relatively sufficient oxygen to the tissue during the process of chronic hypoxia. However, the overproduction of red blood cell (the consequence of chronic hypoxia) now becomes the cause of polycythemia, in which the blood viscosity is high and thus thrombus may be formed in vessels.

## Correlation Between Systemic and Local Regulations

Diseases are generally systemic whereas the local pathological alterations caused by insults are recognized to be representatives of systemic diseases. Local alterations can affect the whole body through