全国高等学校临床医学专业卫生部规划教材英文版

案例分析系列

生物化学

Case Files™ Biochemistry

原　　著　Toy • Seifert • Strobel • Harms

中文主编　贾弘禔　倪菊华

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案例分析系列

出 版 说 明

为贯彻教育部、卫生部关于加强双语教学的精神，配合全国各医学院校开展双语教学的需要以及适应以问题为中心的教学发展趋势，人民卫生出版社特引进了本套案例分析系列英文教材。该教材原版由美国麦格劳希尔教育出版集团出版，在美国各大医学院使用后反响良好。

书中通过剖析临床实例对相关的临床或基础知识进行回顾和复习，有助于医学生将医学基础知识和临床实践相结合。这种以问题为中心的学习(PBL)模式强调发挥学生主动思考的潜力，培养其自我学习能力。在编排上，作者有意将案例顺序随机化，目的是模拟真正的患者就医情景。为方便查询，书后附有以字母为序的案例排列索引。

加入中文编注后的案例分析系列基本保持原书风貌，并根据我国国内教学情况对重要知识点和词汇进行了点评和加注。本套教材语言叙述通俗、简练，即可加强读者对医学知识的理解，又可学习医学英语。

本系列首批教材包括12本：临床医学6本(内科学、外科学、妇产科学、儿科学、精神病学、急诊医学)，基础医学6本(解剖学、生理学、生物化学、微生物学、病理学、药理学)，将于2007年全部推出。

前　言

为适应双语教学的需要，全国高等医药教材建设研究会、卫生部教材办公室和人民卫生出版社在广州召开“全国高等学校医学双语规划教材论证会”（2005年10月9～11日），就相关英文配套教材的编写原则和策略进行了研讨。英文案例分析系列教学丛书——《CASE FILES：BIOCHEMISTRY》（中文注释版，以下简称《注释》）和即将出版的英文版规划教材《BIOCHEMISTRY》（贾弘禔主编，人民卫生出版社，2007）就是根据这个会议精神组织编写的。

英文原版书《CASE FILES：BIOCHEMISTRY》包含46个临床案例（摘要）、临床相关问题，以及疾病相关的生物化学基础知识讨论。为不失原书主题内容和目的，又能满足学生学习英文、掌握相关临床医学和生物化学基础知识的需要，《注释》一书保留全部原有英文病例及相关内容，并对英文病例（摘要）中个别事项额外加了中文注释，同时附英汉名词对照；“点评”是综合了原书介绍的“临床相关问题”（Clinical correlation）和讨论（Discussion），并结合我国当前医学院校用《生物化学》教材中与病例所涉及疾病有关的生物化学基础知识进行的综合叙述。所以，《注释》一书包含了作者对问题的理解和认识，不是原文的翻译。

参加《注释》编写的作者都是北京大学医学部生物化学与分子生物学系的在职青年教师，其中大多数是在近5～8年获得博士学位，有些已经具有高级职称。他们既有医学院校的学习经历，又有一定的临床经历和基础教学经历。对他们来说，编写该书既是学习、提高的过程，又是传授生物化学知识的过程。因此，他们最懂得、理解青年医学读者的需求，有的放矢。希望这本书能成为医学生的好助手，也能帮助那些渴望提升英语专业水平的青年医师。这是我们的初衷。从启动编写到交稿仅有短短的两个月时间，他们利用整个暑假一气呵成。时间仓促，缺点、错误难免，请读者指正。

北京大学医学部　贾弘禔　倪菊华

❖ INTRODUCTION

Often, the medical student will cringe at the "drudgery" of the basic science courses and see little connection between a field such as biochemistry and clinical problems. Clinicians, however, often wish they knew more about the basic sciences, because it is through the science that we can begin to understand the complexities of the human body and thus have rational methods of diagnosis and treatment.

Mastering the knowledge in a discipline such as biochemistry is a formidable task. It is even more difficult to retain this information and to recall it when the clinical setting is encountered. To accomplish this synthesis, biochemistry is optimally taught in the context of medical situations, and this is reinforced later during the clinical rotations. The gulf between the basic sciences and the patient arena is wide. Perhaps one way to bridge this gulf is with carefully constructed clinical cases that ask basic science-oriented questions. In an attempt to achieve this goal, we have designed a collection of patient cases to teach biochemistry related points. More importantly, the explanations for these cases emphasize the underlying mechanisms and relate the clinical setting to the basic science data. We explore the principles rather than emphasize rote memorization.

This book is organized for versatility: to allow the student "in a rush" to go quickly through the scenarios and check the corresponding answers, and to provide more detailed information for the student who wants thought-provoking explanations. The answers are arranged from simple to complex: a summary of the pertinent points, the bare answers, a clinical correlation, an approach to the biochemistry topic, a comprehension test at the end to reinforcement or emphasis, and a list of references for further reading. The clinical cases are arranged by system to better reflect the organization within the basic science. Finally, to encourage thinking about mechanisms and relationships, we intentionally did not primarily use a multiple-choice format. Nevertheless, several multiple-choice questions are included at the end of each scenario to reinforce concepts or introduce related topics.

HOW TO GET THE MOST OUT OF THIS BOOK

Each case is designed to introduce a clinically related issue and includes openended questions usually asking a basic science question, but at times, to break up the monotony, there will be a clinical question. The answers are organized into four different parts:

PART I

1. **Summary**
2. A **straightforward answer** is given for each open-ended question
3. **Clinical Correlation**—A discussion of the relevant points relating the basic science to the clinical manifestations, and perhaps introducing the student to issues such as diagnosis and treatment

PART II

An **approach to the basic science concept** consisting of three parts

1. **Objectives**—A listing of the two to four main principles that are critical for understanding the underlying biochemistry to answer the question and relate to the clinical situation
2. **Definitions of basic terminology**
3. **Discussion of topic**

PART III

Comprehension Questions—Each case includes several multiple-choice questions that reinforce the material or introduces new and related concepts. Questions about the material not found in the text are explained in the answers

PART IV

Biochemistry Pearls—A listing of several important points, many clinically relevant reiterated as a summation of the text and to allow for easy review, such as before an examination

CONTENTS

SECTION I

Applying the Basic Sciences to Clinical Medicine

PART 1. Approach to Learning Biochemistry

PART 2. Approach to Disease

PART 3. Approach to Reading

PART 1. APPROACH TO LEARNING BIOCHEMISTRY

Biochemistry is best learned by a systematic approach, first by learning the **language** of the discipline and then by understanding the **function** of the various processes. Increasingly, cellular and molecular biology play an important role in the understanding of disease processes and also in the treatment of disease. Initially, some of the terminology must be memorized in the same way that the alphabet must be learned by rote; however, the appreciation of the way that the biochemical words are constructed requires an understanding of mechanisms and a manipulation of the information.

PART 2. APPROACH TO DISEASE

Physicians usually tackle clinical situations by taking a history(asking questions), performing a physical examination, obtaining selective laboratory and imaging tests, and then formulating a diagnosis. The conglomeration of the history, physician examination, and laboratory tests is called the **clinical database**. After reaching a diagnosis, a treatment plan is usually initiated, and the patient is followed for a clinical response. Rational understanding of disease and plans for treatment are best acquired by learning about the normal human processes on a basic science level; likewise, being aware of how disease alters the normal physiological processes is understood on a basic science level.

PART 3. APPROACH TO READING

There are six key questions that help to stimulate the application of basic science information to the clinical setting. These are:

1. **What is the most likely biochemical mechanism for the disease causing the patient's symptom or physical examination finding?**
2. **Which biochemical marker will be affected by treating a certain disease, and why?**
3. **Looking at graphical data, what is the most likely biochemical explanation for the results?**
4. **Based on the deoxyribonucleic acid (DNA) sequence, what is the most likely amino acid or protein result, and how will it be manifest in a clinical setting?**
5. **What hormone-receptor interaction is likely?**
6. **How does the presence or absence of enzyme activity affect the biochemical (molecular) conditions, and how does that in turn affect the patient's symptoms?**

1. **What is the most likely biochemical mechanism for the disease causing the patient's symptom or physical examination finding?**

This is the fundamental question that basic scientists strive to answer—the underlying cause of a certain disease or symptom. Once this underlying mechanism is discovered, then progress can be made regarding methods of diagnosis and treatment. Otherwise, our attempts are only *empiric*, in other words, only by trial and error and observation of association. Students are encouraged to think about the mechanisms and underlying cause rather than just memorizing by rote. For example, in sickle cell disease, students should connect the various facts together, setting the foundation for understanding disease throughout their life:

In sickle cell disease, valine(a hydrophobic amino acid) is substituted for glutamate(a charged, hydrophilic amino acid) in the sixth position in the β-globin chain of hemoglobin(Hb). This decreases the solubility of hemoglobin when it is in the deoxygenated state, resulting in its precipitation into elongated fibers in the red blood cell.

This causes the red blood cell to have less distensibility and thus to *sickle*, leading to rupture of the red blood cell(hemolysis) and blockage in small capillaries. The *sludging* in small capillaries leads to poor oxygen delivery, ischemia, and pain.

2. **Which biochemical marker will be affected by therapy?**

After a diagnosis has been made and therapy initiated, then the patient response should be monitored to assure improvement. Ideally, the patient response should be obtained in a scientific manner: unbiased, precise, and consistent. Although more than one physician or nurse may be measuring the response, it should be as carefully performed with little inter-(one person to the next) or intra-variation(one person measuring) as possible. One of the therapeutic measures includes serum or imaging markers; for example, in diabetic ketoacidosis, the serum glucose and pH would be measured to confirm improvement with therapy. Another example would be to follow the volume of a pulmonary mass imaged by CT scan after chemotherapy. The student must know enough about the disease process to know which marker to measure and the expected response over time.

3. **Looking at graphical data, what is the most likely biochemical explanation for the results?**

Medicine is art and science. The **art** aspect consists of the way that the physician deals with the human aspect of the patient, expressing empathy, compassion, establishing a therapeutic relationship, and dealing with uncertainty; the **science** is the attempts to understand disease processes, making rational treatment

plans, and being objective in observations. The physician as scientist must be precise about how to elicit data and then carefully make sense of the information, using up-to-date evidence. Exercises to develop the skills of data analysis require interpretation of data in various representations, such as in tables or on graphs.

4. **Based on the DNA sequence, what amino acid or protein would be produced, and how would the protein be manifest in a clinical setting?**

The clinician-basic scientist collaboration requires each party to "speak the same language" and translate forward and backward from science to clinical, and vice versa. Biochemical thinking is very stepwise, for example, the relationship among DNA, ribonucleic acid (RNA), proteins, and clinical findings. Since the genomic information (DNA) codes for proteins that affect physiological or pathological changes, it is of fundamental importance that the student becomes very comfortable thinking about these relationships:

Forward: *DNA* ➠ *proteins* ➠ *Clinical Manifestations*

Backward: *Clinical Findings* ➠ *proteins effects* ➠ *DNA*

5. **What hormone-receptor interaction is likely?**

A **hormone** is a substance, usually a peptide or steroid, produced by one tissue and conveyed by the bloodstream to another part of the body to effect physiological activity, such as growth or metabolism. A **receptor** is a cellular structure that mediates between a chemical agent (hormone) and the physiological response. The way that the hormone causes its effect is vital to understand, because many diseases occur as a result of abnormal hormone production, abnormal hormone receptor interaction, or abnormal cellular response to the hormone-receptor complex. For example, diabetes mellitus is manifest clinically by high blood-glucose levels. However, in type Ⅰ diabetes (usually juvenile onset), the etiology is insufficient insulin secreted by the pancreas. (Insulin acts to put serum glucose into cells or store it as glycogen.) In contrast, the mechanism in type Ⅱ diabetes (usually adult onset) is a defect of the insulin receptor messenger; in fact, the insulin levels in these individuals are usually higher than normal. Understanding the difference between the two mechanisms allows the scientist to approach individualized therapy, and it allows the clinician to understand the differences in these patients, such as the reason that type Ⅰ diabetics are much more prone to diabetic ketoacidosis (because of insulin deficiency).

6. **How does the presence or absence of enzyme activity affect the biochemical (molecular) conditions, and how does that in turn affect patient symptoms?**

Enzymes are proteins that act as catalysts, speeding the rate at which biochemical reactions proceed but not altering the direction or nature of the reactions. The

presence or absence of these important substances affects the biochemical conditions, which then influence the other physiological processes in the body. Enzyme deficiencies are often inherited as autosomal recessive conditions and may be passed from parent to child. Clearly, when students begin to understand the role of the enzyme and the chemical reaction that it governs, they begin to understand the intricacies of the human biological processes.

BIOCHEMISTRY PEARLS

- There are six key questions to stimulate the application of basic science information to the clinical arena.
- Medicine consists of both art and science.
- The scientific aspect of medicine seeks to gather data in an objective manner, understand physiological and pathologic processes in light of scientific information, and propose rational explanations.
- The skilled clinician must be able to translate back and forth between the basic sciences and the clinical sciences.

REFERENCE

Braunwald E, Fauci AS, Kasper KL et al., eds. Harrison's principles of internal medicine, 15th ed. New York: McGraw-Hill, 2001.

SECTION Ⅱ

Clinical Cases

CASE 1

A 15-year-old African-American female presents to the emergency room with complaints of bilateral thigh and hip pain. The pain has been present for one day and is steadily increasing in severity. Acetaminophen and ibuprofen[注1] have not relieved her symptoms. She denies any recent trauma or excessive exercise. She does report feeling fatigued and has been having burning with urination along with urinating frequently. She reports having similar pain episodes in the past, sometimes requiring hospitalization. On examination, she is afebrile(without fever)and in no acute distress. No one in her family has similar episodes. Her conjunctiva and mucosal membranes are slightly pale in coloration. She has nonspecific bilateral anterior thigh pain with no abnormalities appreciated. The remainder of her examination is completely normal. Her white blood cell count[注2] is elevated at 17,000/mm^3, and her hemoglobin(Hb)[注3] level is decreased at 7.1g/dL. The urinalysis demonstrated an abnormal number of numerous bacteria.

- **What is the most likely diagnosis**?
- **What is the molecular genetics behind this disorder**?
- **What is the pathophysiologic mechanism of her symptoms**?