基础医学专业英语

Professional English of Basic Medicine

主编 崔澂 战庆臣

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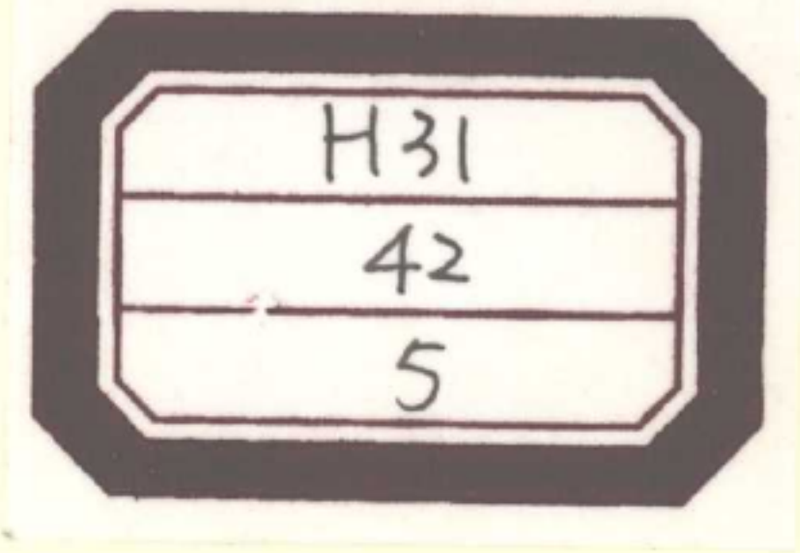
责任编辑　张晓明
封面设计　谷旭升



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崔　澂　战庆臣　主编

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前　言

凡事皆有缘起。编辑本书的缘起则始于长期的医学专业英语教学。

专业英语教学在以往非英语专业高等教育教学中为选修科目，很少受到关注。新《大学英语教学大纲》规定：高等院校非英语专业学生必须修读专业英语，教学时数应不少于100学时。之后，在各高校的课程安排中，专业英语被列为非英语专业学生的必修课目，医学专业学生也是如此。接受教学任务之后，我们决定从已出版的医学专业英语图书中进行综合、比较、选择，然而在遴选过程中发现，尽管已出版的医学英语类的图书教材不下百种，但该类图书或专业内容未能紧跟医学前沿发展，或编写体例简单，或偏重于某单一学科，或偏重于某单一能力培养（以阅读材料汇编类的图书居多），与我们培养高素质通科医学人才目标的教学要求尚有一定距离，于是便产生了编写本书的想法。

在多年实践教学经验的基础上，我们对医学生的英语知识实际需求进行了详细调研，针对目前图书的不足，本书侧重于内容的综合性、前沿性、关联性和实用性四个方面。就综合性而言，本书的12个单元体系完整，涵盖了基础医学的核心课程，并涉及了基础医学的发展方向。就前沿性而言，本书的课文内容尽量做到覆盖学科研究前沿，对在课文中有所涉及又因篇幅所限没能展开的最新内容则通过阅读材料的方式加以补充。就关联性而言，本书在编写中注意与学科的课程设置相配合，编写顺序基本与基础阶段的专业课开设同

步，便于学生在学习过程中与专业学习相互印照，理解提高。就实用性而言，本书体例同时兼顾了各种实用能力的培养，精读课文和阅读材料重在阅读和对医学英语语言的掌握，思考题重在英语语言逻辑和写作能力的提高，对话练习重在听说能力的训练。

编辑此类教材，编者既要具有扎实的英语语言功底，又要具有比较深厚的医学专业知识和教育理论素养。为此，我们要求编者必须具有硕士以上学历，具有较丰富的医学、英语教学和临床医疗经验，并发表过专业论文。参与本书编辑的8位博士、9位硕士不仅符合上述要求，而且均具有强烈的事业心和责任感。在编写过程中，他（她）们精心筛选知识内容，科学安排内容结构，不厌其烦，数易其稿，直至最终定稿。“十年磨一剑”。本书从策划到最后出版用了3年多时间，足见编者的慎重与专注。

在本书编纂过程中，白求恩军医学院刘爱国院长、张宇辉副院长、训练部支国成部长给予了大力支持，并提出了许多指导性意见；主编崔澂博士为本书的最终出版作出了决定性的贡献。当然，我们也深知，一本教材的质量如何，能否达到预期的目标，还有待于实践的检验。我们真诚欢迎来自各方的意见、批评和建议，并表示由衷的谢意，书中失误及不足之处敬请专家评鉴斧正。

编　者

2006年11月

PREFACE

Everything happened has its causes. The cause of compiling this book was the long – term professional medical English teaching.

The teaching of professional English was less concerned because of its status of elective in higher education of non – English major. The new published *The Syllabus of College English* regulates that the students of non – English major in higher schools should choose the professional English as required course, and the time should not less than 100 period. After that, in the courses arrangement of higher schools, English has been the required courses for the students of non – English major, including the students of medical profession. After have taking the teaching task, we decided to choose our text – books from the published professional medical English books. However, during the course of selection, we found that although the published medical books are more than one hundred kinds, they are out of date, simple compiling structures, focusing on some single courses, or emphasizing the training of single capacity, which are not in accordance with the teaching goal of training qualified and all – round graduates. Then the idea of compiling this book occurred to us.

Based on the teaching practice for years, we made a detailed about the practical English need of medical students. Aiming at the shortage of present published books, this book emphasizes particularly on the synthesis, cutting edge of academy, relevancy, and practicability. Considering the synthesis, the 12 units of this book cover almost all the core courses and make a proper introduction on

the frontier of the basic medicine. Considering the cutting edge of academy, this book contains the advanced research result of courses. The latest information which is mentioned in the text and not explained in details can be found in the supplementary reading. Considering the relevancy, cooperating with the setting of the courses, the order of the units is in accordance with the opening of the elementary medical courses. By this way, it is helpful for the students to grasp and understand their professional knowledge. Considering the practicability, the structure of this book takes the training of various practical abilities into consideration. The emphasis of the intensive reading is the reading ability and the grasp of medical English. The dialogue exercise focuses on the training of listening and speaking. The questions' emphasis is the improvement of English language logic. And the summary of the text is mainly about the training of writing.

Compiling a textbook like this, the compilers should not only grasp English well but have the profound medical professional knowledge and educational theory. For this reason, the compilers should be at least master degree, have certain experiences in medicine, English teaching or clinical practice and have published several theses. The compliers of the book, (8 doctors and 9 masters), are not only qualified with the above – mentioned requirements but have strong responsibility. During the compiling period, they circumspectly select the contents, scientifically organize the text structure and patiently modify their script till the final publication. "No pains, no gains". It takes 3 years to plan, compile and publish this book, which entirely shows the compilers' prudence and concentration.

During this period, Liu Aiguo, president of Bethune Military Medical College, Zhang Yuhui, vice – president of the college, and

Zhi Guocheng, director of the training department of the college supported greatly and put forward many instructions. Doctor Cui Cheng, editor in chief, made decisive contribution for the final publication of this book. Of course, we know that only the practice can test the quality of the book and tell us whether the compilers' purposes have been achieved. Different opinions, critiques and advice are welcome and appreciated.

Editors

November 2006

CONTENTS

Unit One

Text

Cell Biology

Modern biology is rooted in an understanding of the molecules within cells and of the interactions between cells that allow construction of multicellular organisms. The more we learn about the structure, function, and development of different organisms, the more we recognize that all life processes exhibit remarkable similarities.

Living systems, including the human body, consist of such closely interrelated elements that no single element can be fully appreciated in isolation from the others. Organisms contain organs; organs are composed of tissues; tissues consist of cells; and cells are formed from molecules. The unity of living systems is coordinated by many levels of interrelationship: molecules carry messages from organ to organ and cell to cell; tissues are delineated and integrated with other tissues by noncellular membranes secreted by cells; and cells gain identity from contacting with other cells. Generally all the levels into which we fragment biological systems interconnect. To learn about biological systems, however, we must take a segment at a time. The biology of cells is a logical starting point because an organism can be viewed as consisting of interacting cells, which are the closest thing to an autonomous biological unit that exists. The integration of cellular activity into tissues, the development of organisms by growth and specialization of cells, and the metabolic events fueling the dynamism

of living systems are all topics on which we will touch, but they are all topics that fall within the province of other subdisciplines of biological science.

The processes of cells were described by cell biologists. That is to say, cell biology investigates how cells develop, operate, communicate, and control their activities. And cell biology also concentrates on the macromolecules and reactions studied by biochemists, the gene control pathways identified by molecular biologists and geneticists. In this millennium, two gathering forces will reshape cell biology: genomics, study of the complete DNA sequence of many organisms, and proteomics, a knowledge of all the possible shapes and functions that proteins employ. Therefore, in order to study the properties of the molecules of life and the innumerable variations on basic themes that are found in different organisms, modern researchers of cell biology employ concepts and experimental techniques drawn from biochemistry, molecular biology and genetics.

Genetics and genetic engineering provide powerful tools for the study of gene function in both cells and organisms. In the classical genetic approach, random mutagenesis is coupled with screening to identify mutants that are deficient in a particular biological process. These mutants are then used to locate and study the genes responsible for that process. Gene function can also be ascertained by reverse genetic techniques. DNA engineering methods can be used to mutate any gene and to re – insert it into a cell's chromosomes so that it becomes a permanent part of the genome. If the cell used for this gene transfer is a fertilized egg (for an animal) or a totipotent plant cell in culture, transgenic organisms can be produced that express the mutant gene and pass it on to their progeny. Many of these methods are being expanded to investigate gene function on a genome – wide

scale. Technologies such as DNA microarrays can be used to monitor the expression of thousands of genes simultaneously, providing detailed, comprehensive snapshots of the dynamic patterns of gene expression that underlie complex cellular processes.

New Words

delineate [di'linieit] v. 描绘

autonomous [ɔ:'tɔnəməs] adj. 自治的

subdiscipline ['sʌb'disiplin] n. （学科的）分支，分科

macromolecule [ˌmækrəu'mɔlikju:l] n. 巨大分子，高分子

biochemist ['baiəu'kemist] n. 生物化学家，生化学家

geneticist [dʒi'netisist] n. 遗传学家

millennium [mi'leniəm] n. 太平盛世，一千年

genomics [ˌdʒi:nə'miks] n. 基因组学

proteomics ['prəutiəˌmiks] n. 蛋白组学

mutagenesis [ˌmjutə'dʒenisis] n. 突变形成，变异发生

chromosome ['krəuməsəum] n. 染色体

genome ['dʒi:nəum] n. 基因组，染色体组

progeny ['prɔdʒini] n. 后裔

simultaneously [siməl'teiniəsly] adv. 同时地

snapshot ['snæpʃɔt] n. 快照，急射，简单印象

Phrases and Expressions

multicellular organism　多细胞机体

starting point　起点

be viewed as　被认为，被看作是

concentrate on　集中于，专注于

molecular biologist　分子生物学家

genetic engineering　遗传工程
transgenic organism　转基因生物
DNA microarray　DNA 微阵列分析

Questions

1. What does cell biology study?
2. How to understand "The unity of living systems is coordinated by many levels of interrelationship"?
3. Why must modern researchers of cell biology employ concepts and experimental techniques drawn from biochemistry, molecular biology and genetics?
4. Make a speech or write a summary about the text.

Dialogue

How to Count the Cells?

Teacher: Good morning, everyone. Today, let's learn about how to count the cells. Well, Tom, could you tell me what we should prepare for it?

Tom: We need a clean count slide or hemacytometer, a clean cover slide, pipet, the culture medium, and a phase – contrast microscope microscope.

Teacher: Good. What should we do first?

Tom: At first, take a count slide or hemacytometer and cover it with a clean cover slide.

Teacher: The count slide and the cover slide should keep clean, otherwise we can't get the exact result. Ok, next step.

Tom: I think we should need pipet and culture medium now. But I

don't know exactly how to do.

Teacher: Take it easy. Dip a 0.1or 1ml pipet into the culture medium, allow a small drop of liquid to form on the end of the pipet, and touch it lightly to the surface of the slide at the periphery of the cover slide. What happen now? Can you see?

Tom: The liquid quickly spread under the cover slide. Then we should need phase – contrast microscope in the next step, am I right?

Teacher: Yeah! Now you should put the slide on the stage of a phase – contrast microscope set to 400. Remember that is 400! And focus on the cells. Are you clear now?

Tom: Fantastic! I got it!

Teacher: Ok! Do it by yourself now.

Reading Material

1. Receptors

Cell surface receptors are able to recognize and bind with high affinity specific subsets of extracellular macromolecules; furthermore, the binding step usually elicits a cellular response. In the case of those receptors, involved in receptor – mediated endocytosis (RME), a major response is the internalization of the ligand. This may be preceded by the generation of a signal that alters cellular metabolism (eg. Polypeptide hormone receptors), or the internalized ligand may be utilized by the cell for specific metabolic needs. In either case, ligand binding is a physiologically important event.

Ligand – receptor interaction is specific and involves only one

family of homologous extracellular molecules and one set of plasma membrane proteins. These receptors usually have been found to be a single protein or protein – protein complex. Moreover, the binding of the specific ligand depends on characteristic ionic and pH conditions. Ligand – receptor interactions have often been further defined by assessing how the specific modification of either the receptor or the ligand inactivates the binding step.

These receptors can therefore be defined by their molecular proteins, the conditions for ligand binding, and their ability to mediate a specific physiologic event. It is this last property that has usually been responsible for their initial detection. For example, LDL receptors were discovered because of their ability to regulate intracellular cholesterol metabolism. Similarily, the asialoglycoprotein receptor and the lysosomal enzyme receptor, to mention two, were first detected as a result of their physiological activity, not their binding properties.

Even though the physiological response is the single most important criterion for establishing the identity of a specific ligand – receptor interaction, often receptor activity must be studied under conditions where the physiologic response cannot be measured. This is particularly true when trying to detect receptors in fractionated cells or in cells that have been treated with fixatives like formaldehyde or gluteraldehyde. In these situations, the identification of receptor activity has to be based on the properties of ligand binding. These properties must be the same as those established for the intact, responsive cell. Thus, it is not sufficient to measure just ligand – specific displaceable binding (the competition between radiolabeled ligand and excess unlabeled ligand for the receptor). Criteria such as time dependence, ionic and chemical requirements, and cell specificity must also be established.

2. Fibroblast – ECM Interaction

In electron micrographs published during the 1960s, people called attention to the very close association of extracellular fibrils, with the cell surface of a number of fibroblast type cells. In oblique sections across the plasmalemma, the extracellular fibrils appeared to be continuous with cytoplasmic cortical materialof the same density, leading to conclude that the cortical material was a precursor of the fibrillar extracellular material, presumed to be collageous. This tendency of extracellular fibrils to coalign with intracellular fibrous components has been rediscovered in recent years by Hynes and Destree, who demonstrated, by double – labeling immunofluorescence, that fibronectin fibrils on the surface of fibroblasts in vitro codistribute with the actin – rich intracellular stress fibers of cells.

Later, Singer confirmed and extended the work of Hynes and others, providing further evidence for a structural connection between extracellular fibronectin fibrils and intracellular bundles of actin filaments in fibroblasts in vitro. Fibronectin fibrils are identified by ferritin – conjugated antibodies. Sections cut oblique to the plasmalemma show that actin filaments subjacent to the fibrils exhibit a collinear arrangement even when the specimen is tilted through 40°. Sections cut perpendicular to the cell surface also show that the fibrous components are collinear. Therefore, we conclude that the extracellular and intercellular components are coaxial and connect with each other in the cell membrane. It seems more likely that a binding protein or receptor in the plasmalemma and/or adjacent cytoplasm actually interconnects the two components.

3. Biosynthesis and Distribution of Organellar Components

Throughout its life, a cell has to deal with the problem of generating and keeping as separate entities a diverse array of organellar membranes and the compartments they circumscribe. Each of these membranes and compartments is endowed with a well - defined set of molecular components: lipids, glycolipids, proteins, glycoproteins, nucleic acids. Furthermore, membrane components have a characteristically asymmetric distribution with respect to the plane of the bilayer. The production of molecules destined to these diverse subcellular membranes and compartments is carried out. So, specific distribution systems must exist, therefore, to ensure that each organellar membrane or compartment receives only its own components, adequately processed, so that it can perform its programmed function. Organellar growth is achieved by the incorporation of new material into a preexisting set of organelles inherited during cell division.

The energy sources, biosynthetic precursors, and enzymes necessary for the synthesis of most organellar proteins and lipids are localized in the cytosol or associated with cytoplasmic side of a specialized membrane, the endoplasmic reticulum (ER) (as a partial exception, mitochondria is able to synthesize some of their own proteins and lipids). Likewise, the enzymes for the synthesis of the dolichol - phosphate - linked oligosaccharide precursor of glycoproteins appear to be also localized on the cytoplasmic side of the ER membrane. In order to reach their final localization and specific orientation in organellar membranes or spaces, proteins and lipids must utilize special transporting systems which assist them in traversing the hydrophobic membrane barriers, and in migrating from

one cell organelle to another. It is believed that specific structural markers or signals in proteins operate as "zip codes," informing the transporting systems of the particular address where the polypeptide is to be delivered. According to this view, proteins sharing a common destination must possess similar "zip codes." Some of these signals have been identified as transient extra peptides found in precursor state of the proteins (or "pre - proteins") such as the hydrophobic, amino terminal sequence of 15 ~ 30 amino acids found in precursors of secretory and integral transmembrane proteins and the extra peptides of cytosolic precursors of some mitochondrial proteins. Other distribution signals may be permanent features of the polypeptide chain, such as those which direct the segregation of ovalbumin into the ER lumen, the insertion of cytochrome P_{450} or the delivery from cytosol to peroxisomes of catalase and uricase. Finally, signals may be added co - or posttranslationally to the proteins as, for example, the mannose - 6 - phosphate residues which direct lysosomal proteins from their site of synthesis, the ER, to the lysosomal compartment.

Different cell membranes acquire their characteristic complement of lipids and these lipids become asymmetrically distributed with respect to the plane of the bilayer. Thus, any model for organelle biogenesis must provide answers to the following key cell biological questions: (1) Where are the different organellar components synthesized? (2) What pathways are used for their distribution to their site of function? (3) What are the sorting signals involved in this distribution? Are they transient or permanent? In the cases of proteins, are they added co - or posttranslationally? How many signals participate in the distribution of a particular component? (4) What are the cellular mechanisms that "read" and "decode" the sorting signals?

参考译文

课　文

细胞生物学

现代生物学源于对构成多细胞有机体的细胞内分子及细胞间相互作用的认识。对不同生物体的结构、功能及发展了解得越多，我们就越发认识到所有的生命过程都呈现出明显的相似性。

生命体，包括人体，都是由相互紧密联系的成分构成的，没有任何一个单一成分能够独立于其他成分而存在。生物有机体包括器官，器官由组织构成，组织由细胞构成，而细胞则由分子构成。生命体这个有机体通过不同层次的相互作用来共同调节：分子在器官与器官、细胞与细胞之间传递信息；组织之间通过细胞膜外分泌途径来表达和整合各种信息；细胞通过彼此相互接触进行信息识别。广义上讲，我们定义的各个层次上的生物系统之间都是相互联系的。为了了解生物体系，我们只能一次选取一个部分进行研究。由细胞生物学开始研究是一个合适的起点，因为生物体可以被看作是由相互作用的细胞构成的，而细胞又是现存最接近可自我调控的生物学单位的研究对象。细胞如何整合形成组织，有机体的发育如何通过细胞的生长和特化进行，新陈代谢如何成为生命体的活力之源，这些都是我们要探讨的问题，并且它们都是生物学的其他分支学科领域所涉及的核心问题。

细胞生物学家主要研究细胞变化过程，即细胞如何发展、发挥作用以及如何调控自身功能。其所关注的领域还包括生物化学家所研究的大分子物质及其反应，及分子生物学家和遗传学家所研究的基因调控途径。在新千年里，两个新学科力量的交汇赋予了细胞生物学崭新的面貌：研究生物完整 DNA 序列的基因组学，以及研究体内蛋白质表现出的所有可能的形态及功能的蛋白组

学。因此，为了研究生命体的分子特性和不同种类生命体中所发现的基于共同特性的不计其数的差异，现代细胞生物学的研究人员采用了生物化学、分子生物学和基因学的理论及实验技术。

遗传学和基因工程为研究细胞和生物中基因的功能提供了强有力的工具。在经典的遗传学研究方法中，随机遗传突变可筛选出某生物学过程中有缺陷的突变型。这些突变型被用来探明和研究相应过程中起作用的基因。基因功能也能通过反义遗传技术确定。DNA 工程可用来使任何基因产生突变，并将其重新插入细胞染色体，从而使突变基因稳定成为基因组中的一部分。如果用于基因转移的细胞是某一动物的受精卵或培养中的多能干细胞，即可产生表达突变基因的转基因生物，并能将此突变基因传递至后代。许多诸如此类的方法在基因组学中被广泛应用于研究基因功能。类似于 DNA 微阵列分析的技术可被用于同时检测上千种基因的表达，快速提供整体细胞活动中作为细胞复杂过程基础的详细、广泛深入的基因动态表达模式。

对　话

如何计数细胞?

老师： 早上好，各位同学。今天我们来学习怎样计数细胞。Tom，你能告诉我要做哪些准备吗?

Tom： 我们需要干净的计数板或血细胞计数器、干净的盖玻片、吸管、培养基和相差显微镜。

老师： 好。首先要做什么?

Tom： 首先，拿出计数板或血细胞计数器，把干净的盖玻片盖在上面。

老师： 计数板和盖玻片需要保持干净，否则我们不能得到准确的实验结果。好，下一步。

Tom： 我认为现在应该用到吸管和培养基。但是我不知道该怎样

做。

老师： 别着急。取 0.1 或 1ml 吸管浸入培养基中，在吸管末端吸取一小滴液体，在盖玻片的边缘轻轻触及载玻片。你现在可以看到发生了什么现象呢？

Tom： 液体迅速扩散到盖玻片下。然后我们要使用相差显微镜了，对吗？

老师： 是的。现在你应该把载玻片放到相差显微镜的载物台上，把显微镜调节到 400 倍。记住是 400 倍。然后开始观察细胞，现在看清楚了吗？

Tom： 太神奇了！我看到了！

老师： 好！你自己再试试。

阅读材料

1. 受体

细胞表面受体能够识别并结合高亲和力特异性细胞外大分子亚单位，结合后通常可引起细胞反应。在那些涉及 RME（受体介导的内吞作用）的受体中，一个主要的反应是腺体内在化。这一反应由可改变细胞代谢（例如，多肽类激素受体）的信号的产生而引起，或是内在化腺体可被用于细胞以供特殊代谢需要。无论是哪种情况，受体与腺体的结合都是重要的生理过程。

腺体－受体相互作用是特异性的，并仅涉及一种同源的细胞外分子家族和一套血浆膜蛋白。这些受体被发现通常是单一蛋白质或蛋白－蛋白复合物。更进一步，受体与特异性腺体的结合依赖离子特性及 pH 环境。腺体－受体相互作用常可通过判断受体或腺体的特异限制性如何灭活相互结合而进一步确定下来。

因此，这些受体可因其分子特性、与腺体结合的条件以及介导特异性生理反应的能力而被确定下来。而最后一个特性常导致受体被最初检测出来。例如，LDL 受体的发现是因为其调节细胞

内胆固醇代谢的能力。与之相类似的两个例子是，缺乏唾液酸类的糖蛋白受体和溶酶体的酶受体第一次被检测出来，是因为其生理功能，而不是它们的结合特性。

虽然生理反应是确定特异性腺体－受体相互作用中最重要的原则标准，我们通常还是要在生理反应不能检测的情况下研究受体活性。这一点在试图从分离细胞或被甲醛固定的细胞中检测受体时特别重要。在这些情况下，受体活性的确定就得建立在与腺体的结合特性基础上。这些特性必须与经完整的具生理反应细胞确定的特性一致。因此，仅通过腺体特异性竞争结合进行检测是不够的（放射性标记腺体和过量未标记腺体与受体之间的竞争结合），诸如时间依赖性、离子、化学物质以及细胞特异性等方面的标准也需要确定。

2. 成纤维细胞－细胞外基质相互作用

在1960s期间发表的电子显微照片中，人们开始注意到细胞外原纤维在许多成纤维细胞表面极其紧密的联系。在沿胞质膜的斜切面上，细胞外原纤维看似与胞浆外层成分呈相同密度的连续性，从而使人们得出结论：胞浆外层成分是原纤维细胞外物质的前体，推测可能是胶原性的。这一有关细胞外原纤维与细胞外纤维状成分并合倾向的观点，后来被 Hynes 和 Destree 通过双标记免疫荧光技术所证实，因为富含生物素的细胞内张力纤维可与成纤维细胞表面纤维结合素性原纤维在体外共同构建。

之后，Singer 证实并拓展了 Hynes 及其他研究人员的工作，进一步体外证实了细胞外纤维结合素性原纤维与成纤维细胞内生物素丝束之间的结构连系。纤维结合素性原纤维可由铁蛋白连接的抗体鉴定。沿胞质膜斜切，观察结果显示，生物素丝与原纤维毗邻，即使将标本以40°斜切，也呈现线性排列。于细胞表面垂直切取标本，纤维性成分亦呈线性排列。因此得出以下结论：细胞外和细胞内成分在细胞膜处相互连接缠绕，有可能胞质膜和/

或相邻细胞浆中的结合蛋白或受体确实与这两种成分互相连系。

3. 细胞器成分的生物合成及分布

贯穿其整个生命过程中，细胞要面临产生及作为独立整体保持一系列不同细胞器膜成分及其局部空间的问题。每一种细胞器膜成分及其内部均含有一整套已确定的分子成分：脂类、糖脂、蛋白、糖蛋白、核酸。另外，膜成分具有特征性的双分子层不对称分布。决定这些种类不同亚细胞膜的组成分子在一些生物合成部位产生出来。因此，必须存在特异性分布系统，以确保每种细胞器膜成分或其内部只接受自身成分，并经适当处理后使其可执行程序化功能。细胞器的发育有赖于在细胞分裂过程中遗传下来的新物质组合进入预先存在的整套细胞器中。

大多数细胞器蛋白和脂类合成所需的能量来源、生物合成前体和酶类多定位在胞液中，或与特定膜结构的胞浆侧内质网（ER）有关（作为特殊例外，线粒体可自身合成一些自身蛋白及脂类）。同样，合成糖蛋白长磷酸链低聚糖前体的酶类也定位于 ER 膜的胞浆侧。为了到达其最终在细胞器膜或某一空间的部位和特异性定位，蛋白和脂类必须使用特殊的转运系统以帮助它们穿过疏水膜屏障，并从一个细胞器迁移至另一细胞器。蛋白中的特异性结构标志物或信号可发挥“密码”的作用，为传递多肽特定位置的转运系统提供信息。按照这种观点，具有同一转运目标的蛋白质须具备相似的“密码”。这些信号中有一些被确认为是处于蛋白质前体状态（或前蛋白）的暂时出现的肽类，例如，在分泌型和完整跨膜蛋白前体中发现的疏水性氨基末端含有的 15～30 个氨基酸序列，以及一些线粒体蛋白的存在于胞液中的前体特殊肽类。其他分布信号具有多肽链长期性的特点，例如，那些可引导卵白蛋白分离进入 ER 腔、细胞色素 P_{450} 的插入或可从胞液转运至含过氧化氢酶和尿酸酶的过氧化物酶体等的信号。最后，信号可于翻译同时或翻译后传至蛋白质，例如，可导

致溶酶体蛋白从其合成部位 ER 到达溶酶体内部的甘露糖 -6- 磷酸残基。

不同的细胞膜需要特征性的脂类成分，这些脂类成分呈非对称性分布以形成双分子层面。因此，任何有关细胞器生物起源的模式，均须回答以下有关细胞生物学的关键问题：（1）不同的细胞器成分是在哪里合成的？（2）这些细胞器成分通过什么途径分布至功能性部位？（3）在其分布中涉及什么分类信号？它们的存在是短暂的还是长期的？对于蛋白质来说，这些信号的介入与翻译同步还是在翻译后进行？在一种特定成分的分布中，有哪些信号参与？（4）“阅读”和“解码”分类信号的细胞机制是什么？

（崔　激　米　裕）

Unit Two

Text

Anatomy

Anatomy is the scientific discipline that investigates the human body's structure and the relationships between body parts. It can be considered at many different levels. Gross anatomy, the study of structures that can be examined without the aid of a microscope, can be approached from either a systemic or regional perspective. In systemic anatomy the body is studied by system. A system is a group of structures that have one of more common functions. In regional anatomy the body is studied by areas. Within each region such as the head or abdomen, all systems are studied simultaneously.

The body can be considered conceptually at seven structural levels: the chemical, organelle, cell, tissue, organ, organ system, and complete organism. The body is considered by most anatomists to have 11 major organ systems: (1) Integumentary system, including skin, hair, nails and sweat glands, whose functions are to protect and regulate temperature, to prevent water loss and produce vitamin D precursors. (2) Locomotor system, including bones, associated cartilage and joint, and muscles attached to the skeleton, whose functions are to protect, support and allow body movement, to produce blood cells and store minerals, to maintain posture and produce body heat. (3) Nervous system, including brain, spinal cord and nerve. It's a major regulatory system of controlling movement, physiological and intellectual functions. (4) Sense system, including different kinds of sensory receptors. It's a major regulatory system of detecting sensation, controlling physiological functions. (5) Endocrine system, including different endocrine glands such as the pituitary, thyroid and adrenal glands. It can participate in the regulation of metabolism, reproduction, and many other functions. (6) Cardiovascular system, including heart, blood vessels, blood and lymph organ. It can transport nutrients, waste products, gases and hormones throughout body, maintain tissue fluid balance and absorb fats, meanwhile plays a role in the regulation of body temperature. (7) Immunol system, including bone marrow, thymus, spleen, lymph nodes and other lymph organs. It can remove foreign substances from the blood and lymph, combat disease through immune response. (8) Respiratory system, including lungs and respiratory passages, exchanges gases (oxygen and carbon dioxide) between the blood and the air and regulates blood pH. (9) Digestive system, including mouth, esophagus, stomach, intestines and accessory structure,

performs the mechanical and chemical processes of digestion, absorption of nutrients and elimination of wastes. (10) Urinary system, including kidneys, urinary bladder and ducts that carry urine, removes waste products from the circulatory system, regulates blood pH, ion balance and water balance. (11) Reproductive system, including gonads, accessory structures and genitals of males and females, performs the processes of reproduction and controls sexual function and behaviors.

When describing parts of the body, directional terms is often important to refer to their relative anatomical positions, regardless of its actual position. The anatomical position refers to a person standing erect with the feet facing forward, arms hanging to the sides, and palms facing forward. Right and left are retained as directional terms in anatomical terminology. Up is replaced by superior, down by inferior, front by anterior, and back by posterior. The important directional terms include: Cephalic (cranial, closer to the head than another structure, usually synonymous with superior); Caudal (closer to the tail than another structure, usually synonymous with inferior); Ventral (towards the belly, synonymous with anterior); Dorsal (toward the back, synonymous with posterior); Proximal (closer to the point of attachment to the body than another, usually used to refer to limbs); Distal (farther from the point of attachment to the body than another structure, usually used to refer to limbs); Lateral (away from the midline of the body); Medial (toward the midline of the body); Superficial (toward or on the surface); Deep (away from the surface).

At times it is conceptually useful to describe the body as having imaginary flat surfaces called planes passing through it. A plane divides or sections the body, making it possible to "look inside" and

observe the body' structures. A sagittal plane runs vertically through the body and separates it into right and left portions. A midsagittal or a median plane divides the body into equal right and left halves. A transverse of horizontal plane runs parallel to the ground and divides the body into superior and inferior portions. A frontal or coronal plane runs vertically from right to left and divides the body into anterior and posterior part. Additionally, organs are often sectioned to reveal their internal structure. A cut through the long axis of the organ is a longitudinal section, and a cut at right angles to the long axis is a cross, or transverse section.

New Words

anatomy [ə'nætəmi] n. 解剖学
organelle [ˌɔ:gə'nel] n. 细胞器
integumentary [in,tegju'mentəri] adj. 体被的，皮的
precursor [pri (:)'kə:sə] n. 先驱；先兆，预兆；前体
cartilage ['ka:tilidʒ] n. 软骨
spinal ['spainl] adj. 脊柱的，脊髓的
endocrine ['endəukrain] n. 内分泌
pituitary [pi'tju (:) itəri] n. 垂体
thyroid ['θairɔid] n. 甲状腺
metabolism [me'tæbəlizəm] n. 新陈代谢
cardiovascular [ˌka:diəu'væskjulə] adj. 心血管的
thymus ['θaiməs] n. 胸腺
esophagus [i (:)'sɔfəgəs] n. 食道
intestine [in'testin] n. 肠 adj. 内部的，国内的
urinary ['juərinəri] adj. 尿的，泌尿器的
kidney ['kidni] n. 肾

gonad [ˈgɔnæd] n. 性腺，生殖腺
genitals [ˈdʒenit（ə）lz] n. 生殖器（尤指男性外生殖器）
inferior [inˈfiəriə] adj. （位置）下方的
anterior [ænˈtiəriə] adj. 前面的，在前的
posterior [pɔsˈtiəriə] adj. 后面的
cephalic [seˈfælik] adj. 头端的
cranial [ˈkreinjəl] adj. 颅侧的
synonymous [siˈnɔnimәs] adj. 同义的
caudal [ˈkɔːdl] adj. 尾部的，近尾部的
ventral [ˈventrəl] adj. 腹侧的，腹的，腹部的
dorsal [ˈdɔːsəl] adj. 背侧的，背的
proximal [ˈprɔksiməl] adj. 近侧的，最接近的
distal [ˈdistəl] adj. 远侧的，末梢的
lateral [ˈlætərəl] n. 侧部 adj. 外侧的
medial [ˈmiːdjəl] adj. 中央的；n. 中部
superficial [sjuːpəˈfiʃəl] adj. 表面的，浅的
section [ˈsekʃən] n. 切开（术）；切面，截面；切片
sagittal [ˈsædʒitl] adj. 矢状的，径向的
transverse [ˈtrænzvəːs] adj. 横向的，横断的
frontal [ˈfrʌntl] n. 额状的，前沿的
coronal [ˈkɔrənl] adj. 冠状的
axis [ˈæksis] n. 轴
longitudinal [lɔndʒiˈtjuːdinl] adj. 纵向的

Phrases and Expressions

gross anatomy　大体解剖学
systemic anatomy　系统解剖学
regional anatomy　局部解剖学
endocrine gland　内分泌腺

adrenal gland　肾上腺
lymph node　淋巴结
urinary bladder　膀胱
sagittal plane　矢状面
frontal (or coronal) plane　额状面或冠状面
longitudinal section　纵切面
cross (or transverse) section　横切面

Questions

1. What is the purpose of the gross anatomy, systemic anatomy and regional anatomy, respectively?
2. How many major organ systems are there in the body? And how about their main functions?
3. Please describe the directional terms as many as you can.
4. How to describe the relationship between thymus and chest cavity in directional terms?
5. Make a speech or write a summary about the text.

Dialogue

Examination

Teacher: And now, it's you turn.

Tony: Oh… yeah, but I am a little nervous…

Teacher: Please take it easy. They are not very difficult problems. Try it!

Tony: Well, I'll do my best.

Teacher: Ok, Let's begin. Describe in as many directional terms as

you can the relationship between your kneecap and heel.

Tony: My kneecap is both proximal and superior to the heel. It is also anterior to the heel because it is on the anterior side of the lower limb, whereas the heel is on the posterior side.

Teacher: Very good. Please name the three parts of the pharnx.

Tony: The pharynx consists of three parts: the nasopharynx, the oropharnx, and the laryngopharynx.

Teacher: Good job. What are the functions of the digestive system?

Tony: Performing the mechanical and chemical processes of digestion, absorption of nutrients, and elimination of wastes.

Teacher: Now tell us the location of the liver.

Tony: It is in the right upper quadrant of the abdomen.

Teacher: Ok, wait a moment. Let's shift the topic. Yes, here … Please describe the effect that a lesion in the right optic nerve would have on the visual fields.

Tony: A lesion in the right optic nerve results in loss of vision in the right visual field.

Teacher: Lesions of the dorsal column – medial lemniscal system in the spinal cord (dorsal column) cause loss of proprioception, fine touch, and vibration on the same side of the body below the level of the lesion. Lesions of the dorsal column – medial lemniscal system above the level of the medulla oblongata cause the same loss on the opposite side of the body below the level of the lesion. Explain why.

Tony: Lesions of the dorsal column – medial lemniscal system in the spinal cord (dorsal column) result in loss of proptioception, two – point discrimination, and vibration on the same side of the body below the lesion result from the dorsal column terminating in the nucleus gracillis and cuneatus without

crossing over to the other side of the spinal cord. However, fibers from the nucleus gracilis and cuneatus decussate and enter the medial lemniscus. Lesions of the medial lemniscus result in loss on the opposite side of the body.

Teacher: Unilateral damage to the hypoglossal nerve results in loss of tongue movement on one side, which is most obvious when the tongue is protruded. If the tongue is deviated to the right, would the left or right hypoglossal nerve be damaged?

Tony: The tongue is protruded by contraction of the geniohyoid muscle, which pulls the back of the tongue forward, pushing the muscle mass of the tongue forward. With one side pushed forward and unopposed by muscles of the opposite side, the tongue deviates toward the nonfunctional side. Therefore in the example the right hypoglossal nerve is damage.

Teacher: Excellent!

Reading Material

1. Movements at Joints

From the anatomical position forward movements about a transverse axis are called flexion and backward movements are called extension. Forward bending of the head on the neck, the neck on the trunk and the trunk on the hips are called flexion, as are forward raising of the upper arm at the shoulder joint, forward bending of the forearm at the elbow, of the hand at the wrist and the fingers into the palm. Similarly forward raising of the lower limb at the hip is flexion. A

change takes place lower down the lower limb. Backward bending of the leg at the knee, downward movement of the foot at the ankle and bending downwards of the toes are also flexion movements although the movements of the foot and toes are better referred to as plantar flexion. All the opposite movements are called extension but a better term for those of the foot and toes is dorsiflexion.

Abduction is a movement away from the midline about an antero-posterior axis and adduction is a movement towards the midline about the same axis. The upper limb can be abducted through 180° from the side of the body to a position alongside the head. There is no abduction at the elbow and the hand can be abducted at the wrist to a limited extent. Abduction of the lower limb at the hip to about 60° is possible but there is no abduction at the knee and ankle. Adduction of the upper limb is restoration of the abduction limb or bringing the upper limb across the front or back of the chest. Adduction of the hand at the wrist is much more extensive than abduction. The lower limb can be adduction at the hip by bringing it across the front of the other limb.

Rotatory movements take place about a longitudinal axis, and are possible at the shoulder and hip joints because they are ball and socket joints. In rotation the anterior surface of the limb is turned laterally and in medial rotation it is turned medially. In the forearm the radius can rotate medially and cross over the ulna. This is called pronation. The opposite movement which brings the radius back to its position parallel and lateral to the ulna is called supination. The head can rotate together with the atlas on the axis to the right and to the left. The trunk can be rotated to the right and to the left because each vertebra can rotate a little on the neighboring vertebra.

2. The Arteries and Veins of the Heart

The heart is supplied with blood by the right and left coronary arteries that arise from the aorta just above its origin from the left ventricle. The right coronary artery passes forwards between the right auricle and pulmonary artery and then winds round to the right in the coronary sulcus to the back of the heart. The left coronary appears between the left auricle and the pulmonary artery and winds round to the left in the coronary sulcus to the back of the heart. The two arteries meet in this groove posteriorly.

Both arteries give off large branches. Both the main arteries and the large arteries have very few anastomoses with each other. The word anastomosis refers to connecting arterial channels between arteries before they break up into capillaries. These channels can be of great importance because if an artery is blocked the part supplied by it may obtain blood from an alternative source. Arteries which have no anastomoses are called end arteries, that is, they have no connexion with other arteries before they form capillaries. These are found in the grey matter of the cerebral cortex, the spleen, the kidneys and the lungs. The occlusion of a coronary artery or one of its large branches leads to sudden death. Partial occlusion leads to a condition called angina pectoris which is characterized by pain over the sternum on exertion.

The veins of the heart join the coronary sinus which opens into the right atrium. These are many small veins opening directly into the right atrium.

3. The Trachea

The trachea is about 10 cm long about 2 cm wide and extends from the sixth cervical vertebra to the fifth thoracic vertebra where it divides into the right and left main bronchi. It lies mainly in the midline but where it divides it lies slightly to the right. It is more or less circular but is flattened behind. In the neck, it is relatively superficial and its rings can be felt above the manubrium sterm. In the thorax it lies much more deeply behind the arch of the aorta. Behind it, along its whole length, is the oesophagus. On either side are the large vessels of the neck. The isthmus of the thyroid gland crosses the second, third and fourth tracheal rings.

There are about twenty incomplete rings of cartilage in the trachea. The rings are defective posterior. The rest of the wall consists of connective tissue and smooth muscle and the trachea is lined by a ciliated, mucous, columnar epithelium. The walls of the trachea to some extent and both its length and width can be varied, for example, on inspiration the trachea is lengthened. The main function of the trachea is to provide a passage for air during respiration and the rings maintain its patent.

参考译文

课　文

解剖学

解剖学是一门研究人体结构及其毗邻关系的科学，可以从许多不同的水平来认识。大体解剖学是不借助显微镜研究结构的科学，可按照系统或局部进行。系统解剖学按系统研究人体，一个

系统由许多功能相同的结构组成。局部解剖学按照部位研究人体。在每个部位，如头部或腹部等，所有的系统结构被同时研究。

人体从概念上可分为7个结构水平：化学组分、细胞器、细胞、组织、器官、系统和整个机体。多数解剖学家认为人体有11个系统：（1）体被系统，包括皮肤、毛发、指（趾）甲和汗腺，其主要功能是保护和调节体温、防止水分丢失、产生维生素D前体。（2）运动系统，包括骨、软骨和关节，以及附着在骨骼上的肌肉，其主要功能是保护、支持、运动，产生血细胞和贮存矿物质，保持姿势及产生体热。（3）神经系统，包括脑、脊髓和神经，是人体的主要调节系统，可控制运动、生理功能和智能。（4）感觉系统，包括各种类型的感受器，是人体的主要调节系统，可探测感觉，调控生理功能。（5）内分泌系统，包括各种内分泌腺，如垂体、甲状腺和肾上腺等，参与新陈代谢、生殖和许多其他功能的调节。（6）心血管系统，包括心脏、血管、血液和淋巴器官，可运输全身的营养物质、代谢废物、气体和激素，保持组织液平衡，转运脂肪，并在体温调节中发挥作用。（7）免疫系统，包括骨髓、胸腺、脾脏、淋巴结和其他淋巴器官，可通过免疫反应清除血液和淋巴中的异物，抗击疾病。（8）呼吸系统，包括肺和呼吸道，可在血液和空气之间进行气体交换（氧和二氧化碳），调节血液pH值。（9）消化系统，包括口腔、食管、胃、肠及附属结构，可进行机械和化学消化过程，吸收营养物质，排出废物。（10）泌尿系统，包括肾、膀胱及排尿管道，从循环系统中清除代谢废物，调节血液pH值、离子平衡和水平衡。（11）生殖系统，包括生殖腺、附属结构和男女外生殖器，主司繁殖，控制性功能和性行为。

当描述人体各个部位时，可代表其相对解剖学位置的方位术语非常重要。解剖学姿势是指人体直立，两足向前，两臂下垂于身体两侧，手掌向前。右和左仍用做解剖学方位术语。superior

代替上，inferior 代替下，anterior 代替前，posterior 代替后。重要的方位术语包括头侧（颅侧，近头者，与上同义）；尾侧（近尾者，与下同义）；腹侧（近腹部者，与前同义）；背侧（近背部者，与后同义）；近侧（距附着于躯体部位近者，通常用于四肢）；远侧（距附着于躯体部位远者，通常用于四肢）；外侧（距人体正中面远者）；内侧（距人体正中面近者）；浅（距体表近者或位于体表者）；深（距体表远者）。

很多时候需要用通过人体的、叫做面的假想平面来描述人体。面分开或切开人体，使从内部观察人体结构成为可能。矢状面垂直纵切人体，将人体分为左、右两部分。正中矢状面或正中面将人体分为左、右相等的两半。横切面或水平面与地面平行，将人体分为上、下两部分。冠状面或额状面从左、右方向纵切人体，将人体分为前、后两部分。另外，经常会切开器官以观察其内部结构。沿器官长轴的切面称纵切面，垂直于器官长轴的切面称横切面。

对　话

考试

老师： 现在该你了。

Tony： 哦……，好吧，可是，我有点儿紧张……

老师： 别着急。这些不是很难的问题。尽力而为！

Tony： 我试一试。

老师： 好，开始。请用尽可能多的方位术语描述膝盖和脚后跟的位置关系。

Tony： 膝盖位于脚后跟的近侧和上方。膝盖也位于脚后跟的前方，因为膝盖位于下肢的前面，而脚后跟位于下肢的后面。

老师：很好！请说出咽的三个部分。

Tony：咽由三部分组成：鼻咽、口咽和喉咽。

老师：不错！消化系统的功能是什么？

Tony：进行机械和化学消化过程，吸收营养物质，排出废物。

老师：肝的位置在哪？

Tony：肝位于右上腹部。

老师：好，等一会，咱们换一个题目。噢，这儿……请描述右侧视神经损伤后对视野造成的影响。

Tony：右侧视神经损伤会造成右侧视野全盲。

老师：脊髓（后索）内的后索－内侧丘系损伤，导致损伤平面以下同侧躯体本体觉、精细触觉和振动觉丧失。延髓水平以上的后索－内侧丘系受损，导致受损平面以下对侧躯体出现同样的感觉丧失。解释为什么？

Tony：脊髓（后索）内的后索－内侧丘系损伤导致损伤平面以下同侧躯体本体觉、两点辨别觉和振动觉丧失，是因为后索的纤维在终止于薄束核和楔束核之前，在脊髓的同侧上升，不交叉至脊髓的对侧。但是，薄束核和楔束核发出的纤维交叉至对侧，形成内侧丘系，因而内侧丘系损伤导致对侧躯体出现感觉丧失。

老师：一侧舌下神经损伤，导致同侧舌肌运动障碍，尤其在伸舌时最明显。若舌头偏向右侧，是左侧还是右侧舌下神经受损？

Tony：颏舌骨肌收缩时，推动舌的后部向前，进而推动整个舌肌向前，使舌伸出。在一侧舌肌向前推，而失去对侧舌肌的拮抗作用时，舌偏向瘫痪侧。因此，本例是右侧舌下神经受损。

老师：非常好！

阅读材料

1. 关节的运动

从解剖的位置来看，沿横轴向前的运动称为屈曲，向后则称为伸展，头在颈之上、颈在躯干之上或躯干在髋之上的前屈，都称为屈曲。上肢在肩关节处的前举，前臂在肘部、手在腕部的前屈，以及手指握向手掌，亦是如此。同样的，下肢在髋关节向上举起，也是屈曲。而在下肢的下段，情况就发生了变化。小腿在膝向后屈，足在踝关节向下运动以及足趾的下屈，也是屈曲运动，而足与足趾的这种运动，称之为跖屈更恰当。所有反方向运动称为伸展，但适用于足和趾的更好名称是背屈。

外展是在前后轴附近离开正中线的运动，而内收则是在同一个轴附近靠拢正中线的运动。上肢能从体侧外展 180 度，处于与头靠拢的位置。肘关节无外展活动，手在腕部有一定限度的外展活动。下肢从髋关节可能做 60 度的外展，而膝和踝关节则不能外展。上肢的内收是已处于外展的肢体复位，或使上肢越过胸的前面或背侧。下肢的内收，是在髋关节处使它跨过另一下肢的前方。

旋转运动发生在纵轴：可能是在肩关节和髋关节，因为它们是球－窝关节。侧旋时，肢体的前部转向外侧；内旋时，则转向内侧。在前臂，桡骨能向内旋转，并跨过尺骨，这称为旋前。反方向的运动，即令桡骨回复到它与尺骨平行的外侧位，则称为旋后。头与寰椎能在枢椎上一起向左、右转动。躯干能向左、右转动，因为每一个椎体能在毗邻的椎体上稍微转动。

2. 心脏动静脉

心脏的血液供应来自左、右冠状动脉，它们的起源恰位于主动脉在左心室起点的上方。右冠状动脉在右心耳和肺动脉之间通向前方，然后在冠状沟内蜿蜒绕向右侧到达心脏背面。左冠状动

脉始于左心耳和肺动脉之间，在冠状沟内蜿蜒绕向左侧到达心脏背面。两支动脉在此沟后面吻合。

两支动脉均分出大的分支，均与大动脉之间只有极少的吻合支。所谓吻合支，是指在形成毛细血管之前，介于动脉之间的交通管道。这些交通支十分重要，因为当一支动脉阻塞时，就可以从其他交通支获得血液供应。无吻合支的血管称为终末动脉，也就是说，这种动脉在形成毛细血管之前，与其他动脉之间无连接。终末动脉可存在于大脑皮层的灰质、脾脏、肾脏和肺。冠状动脉或它的一条大分支闭塞可导致猝死。部分闭塞可导致心绞痛，其特征是在劳累时出现胸骨区疼痛。

心脏静脉连接于冠状静脉，其开口入右心房，另尚有许多小静脉直接开口入右心房。

3. 气管

气管长约 10 厘米、宽约 2 厘米，从第 6 颈椎延伸到第 5 胸椎，并在此分成左、右主支气管。总的来说，它位于正中线，但在其分叉处，则稍偏右侧。它的轮廓大致呈环形，但在后面是扁平的。在颈部，气管相对较表浅，并且它的环能够在胸骨柄的上方扪到。在胸部，它的位置深得多，位于主动脉弓的后面，整个气管的后面是食管，在它的两侧是颈部大血管，甲状腺峡部则跨越第 2、3 和 4 气管环。

气管有大约 20 个不完全的软骨环，环的后面有缺损。气管壁的其余部份由结缔组织和平滑肌组成，管壁内侧为纤毛柱状粘膜上皮。气管壁的长度和宽度在一定范围内可发生改变，例如，吸气时气管伸长。气管的主要功能是在呼吸时为空气提供通道，气管环则保持气管的通畅。

（张　峰　樊宇兵）

Unit Three

Text

Histology and Embryology

Histology is a term derived from the Greek *histos*, meaning tissue, and *logia*, meaning the study of or knowledge. And since histology refers to the study of cells, tissues, and organ systems, it embraces a study of function as well as structure. Thus, a study of histology not only formed the complement to the study of gross anatomy, it also provided a structural basis for the study of physiology. The correlation between structure and function perhaps provides the reason why histology is such an intriguing and readily understandable subject. Knowledge of the normal is a necessary prelude to the study of the abnormal (pathology), which deals with the alterations in structure and function of the body and of its organs, tissues, and cells caused by disease. Hence, the study of histology is fundamental within the medical and dental curriculum. Students should find that if they examine a structure, they can deduce much about its function; conversely, if they know the function of an organ or tissue, they can forecast much of its microscopic structure.

The tissues of the body are assigned to four principal types on the basis of structure and function. (1) Epithelial tissue, covers body surface, lines body cavities and ducts, and forms glands. (2) Connective tissue, binds, supports, and protects body parts. (3) Muscle tissue, contracts to produce movement. (4) Nervous tissue, initiates

and transmits nerve impulses from one body part to another.

Histology is a meeting – place of anatomy, biochemistry, and physiology. Learning the microscopic structure of the human body completes the study of gross anatomy. Biochemistry deals with the chemical compounds and the chemical processes in living things. However, chemical molecules, eg. enzymes, nucleic acid, glycogen and lipids, do not float randomly in solution in the body. They are precisely organized inside the cells and tissues into discrete structures. Each type of cell and tissue and each organ are specially adapted to perform one particular function. Pathology is the study of the cause and effects of the disease and deals with the alteration brought about by disease in the structure and function of the body and of its organs, tissues and cells. An understanding of normal microscopic structure is a necessary prelude to the study of pathology. It is impossible to study the abnormal before the normal is unknown. Although most medical student are not going to become histologists, a thorough knowledge is of histology fundamental for them as future doctors.

Of all problem in biology, none are more challenging than those of development – the mechanism whereby. Under the guidance of the genes, there emerges from a single – celled beginning to an integrated multi – celled organism, developing organisms follow specific patterns of growth and differentiation that are genetically programmed long before expression occurs. The techniques of molecular biology, genetics, biophysics, physiology, immunology, and ultra – structural analysis are used to study development stages of differentiation, growth, and morphogenesis in a variety of organisms. So, embryology which studies the development of human body also has more and more closer relationships with other disciplines.

The early stage of embryonic development is: fertilization and the formation of the zygote, the morula at about the third day, early blastocyst forms at the time of implantation between fifth and seventh day, at three weeks the blastocyst shows the three germ layers that constitute the embryonic disc. During the development and growth of embryo, some harmful factors can result in abnormal development. At last, deformed even dead embryo will occur. Therefore, it is also important for medical students to study embryology in order to understand innate diseases of clinical departments.

New Words

intriguing [in'tri:giŋ] αdj. 引起兴趣（或好奇心）的；有迷惑力的

readily ['redili] adv. 乐意地；很快地；无困难地

prelude ['prelju:d] vi. 作序曲，作序言 n. 先驱，前奏，序幕

deduce [di'dju:s] vt. 演绎，推演，推断

glycogen ['glaikəudʒen] n. 肝糖原

lipid ['lipid] n. 类脂

precisely [pri'saisli] adv. 精确地，明确地

discrete [dis'kri:t] adj. 不连续的，离散的

emerge [i'mə:dʒ] v. 显现，出现，暴露

biophysics ['baiəu'fiziks] n. 生物物理学

morphogenesis [mɔ:fə'dʒenisis] n. 形态发生，形态形成

fertilization [ˌfə:tilai'zeiʃən] n. 受精，施肥

zygote ['zaigəut] n. 受精卵

morula ['mɔ:rjulə] n. 桑葚胚

blastocyst ['blæstəusist] n. 胚泡

Phrases and Expressions

derive from　源于，来自于

gross anatomy　大体解剖学

be assigned to　被指定为……，被划分为……

nucleic acid　核酸

germ layer　胚层

embryonic disc　胚盘

Questions

1. What do histology and embryology study?
2. How many types are the tissues of the body divided into?
3. How to understand the relationship between histology and pathology?
4. How does the early embryo develop?
5. Make a speech or write a summary about the text.

Dialogue

1. Basic Knowledge of Using Light Microscope

Teacher: Light microscope is one of the elementary tools of histology study. *Before beginning the experiment, let's recall the use* of light microscope firstly. Look at the microscope in front of you, how can you move it correctly? Put up your hands! Tony, please.

Tony: Hold the arm of the microscope with the right hand.

Teacher: That's enough? Think for a while. What about left one? (Reminding him with gesture)

Tony: Oh, I see. We should hold the base in the left palm at the

same time.

Teacher: Well done. Sit down please. Next, where should we rest a specimen? Alice, please.

Alice: On the stage.

Teacher: Ok. Then, how can we move the specimen?

Alice: Move the specimen pusher.

Teacher: Very good. Sit down please. Attention! We shouldn't move the specimen by hand in this kind of microscope. Now turn on the light source of your microscope, not too bright. Place the specimen on the stage. Move the object into position beneath the objective lens. Which is the objective lens, you know?

Students: Yes!

Teacher: Good. Then how can we make the image present clearly? Tom, please.

Tom: Turn the knobs beside the arm to up or down the stage.

Teacher: Right. The knobs are the coarse and fine adjustment. Then, if you have found the image but not clearly enough, what should you do?

Tom: Well, regulate the fine adjustment.

Teacher: Certainly. As medical freshmen, in order to learn histology well, you must be familiar with the use of the light microscope.

2. About HE Staining

Teacher: Look at the electronic picture, what kind of specimen is it? Surely, it's for light microscope. Ok, Alice, please.

Alice: I think it is a paraffin section of the urinary bladder.

Teacher: You' re correct. Paraffin section is the most classical technology and in common use. Then what' s the conventional staining method for paraffin sections?

Alice: The hematoxylin – eosin staining.

Teacher: HE staining for short. Good job. Sit down please. What about the characteristic of HE staining? Oh, Bob, don't you try?

Bob: Well…

Teacher: Take it easy. Don't be afraid of making mistakes. Look at the cells in the picture.

Bob: Oh, It's stained blue and red.

Teacher: Ok, observe carefully, the nucleus is…

Bob: The nucleus is stained purplish blue and the plasma red.

Teacher: Quite right. Sit down please. Staining increases inherent contrast of the specimen and makes it clearly to observe. So you should master the feature of HE staining, which will help you to understand the structure of cells and tissues easily.

Reading Material

1. Stem Cell Bioengineering

Tissue engineering and cellular therapies, either on their own or in combination with the therapeutic gene delivery, have the significantly potential impact on medicine. Implementation of technologies based on these approaches requires a readily available source of cells for the generation of cells and tissues outside a living body. Because of their unique capacity to regenerate functional tissue for the lifetime of an organism, stem cells are an attractive " raw material" for multiple

biotechnological applications. By definition, they are self – renewing because differentiate into numerous specialized, functional cells. Recent findings have shown that stem cells exist in most, if not all, tissues, and that tissue may be more flexible than originally thought. Although the potential for producing novel cell – based products from stem cells is large, currently there are no effective technologically relevant methodologies for culturing stem cells outside the body, or for reproducibly stimulating them to differentiate into functional cells. A mechanistic understanding of the parameters important in the control of stem cell self – renewal and lineage commitment is thus necessary to guide the development of bioprocesses for the ex vivo culture of stem cells and their derivates.

2. Stem Cell Repair of Central Nervous System Injury

Neural stem cells (NSCs) have great potential as a therapeutic tool for the repair of many CNS disorders. Large – scale sources of neural stem cells are crucial for both basic research and novel approaches toward treating neurological disorders. NSCs can be isolated from embryonic and adult brain tissue, be induced from oncogene immortalized stem cells, or both mouse and human ES cells. Cells including multiple subtypes of CNS and PNS neurons, as well as oligodendrocytes, Schwann cells, and astrocytes, are modeled by these large – scale sources.

NSCs proliferate in vitro through many passages without losing their multipotentiality. Following engraftment into the adult CNS, NSCs differentiate mainly into glia, except in neurogenic areas. After engraftment into the injured and diseased CNS, their differentiation is

further retarded. In vitro manipulation of NSC prior to transplantation and/or modification of the host environment may be necessary to control the terminal lineage of the transplanted cells to obtain functionally significant numbers of neurons. NSCs and a few types of glial precursors have shown the capability to differentiate into oligodendrocytes and to remyeliate the demyelinated axons in the CNS, but the functional extent of remyelination achieved by these transplants is limited. Manipulation of endogenous neural precursors may be an alternative therapy or a complimentary therapy to stem cell transplantation for neurodegenerative disease and CNS injury. However, this at present is challenging and so far has been unsuccessful. Understanding mechanisms of NSC differentiation in the context of the injured CNS will be critical to achieving these therapeutic strategies.

3. Cardiac Tissue Engineering: Characteristics of in Unison Contracting Two – and Three – dimensional Neonatal Rat Ventricle Cell (co) – cultures

Patients with heart failure have, in spite of improved palliative therapies, bad prognosis. Cardiac tissue engineering by use of a temporary bioscaffold and cardiomyocytes may help to find answers for future treatments in heart failure. For that purpose two neonatal rat heart ventricular cell fractions were obtained after a gradient cell separation. Time related characteristics of Fractions I and II were established in two – dimensional (2 – D) and three – dimensional (3 – D) cell cultures. The 3 – D cardiac constructs were obtained by use of a bovine type I collagen matrix after culturing either under static conditions or in the HARV bioreactor. With the 2 – D cultures

contracting cells were present after 1 day, and reached confluency from day 5 on and this was maintained up to 135 days. In Fraction – I some non – contracting cells were always noticed between the (in time in unison) contracting cells. Transmission electron microscopy (TEM) revealed that these mainly concerned fibroblasts. Differences in the expression of alpha – SM – 1 actin and troponin – T were observed between the two fractions. In both fractions endothelial cells and macrophages were only sporadically observed. All through the 3 – D matrix pendant – like single cell and clustered cell contractions were present after 1 ~ 2 days, resulting in time in unison contracting of cells with the collagen matrices. The whole event was faster with Fraction – I and was observed up to 3 weeks. At this time point clusters of troponin – T positive cells were found scattered through the collagen matrices. Additionally, TEM revealed healthy layers of connected cardiomyocytes with intercalated discs, in this case on and in between the collagen fibres. These findings provide evidence that in unison contracting structurally organized cell – matrix cardiac constructs can be engineered by use of co – cultures (neonatal cardiomyocytes and fibroblasts) and collagen matrices, which is very promising for the repair of larger scar areas of the myocardium.

参考译文

课　文

组织学与胚胎学

Histology 这个词源于希腊语 *hitos*（组织）和 *logia*（研究或知识）。由于组织学的研究涉及细胞、组织和器官系统，所以除了研究它们的结构外，也研究其功能。因此，它不仅对大体解剖

学的研究提供补充，还为生理学的研究提供结构基础。或许是由于结构与功能的互相联系，使得组织学成为极具吸引力和易于理解的学科。掌握正常结构是学习非正常结构（病理）的必要前提，后者则是有关由疾病引起的机体及其器官、组织、细胞结构及功能的变化。所以，组织学是医学和口腔学科必不可少的基础课程。学生们会发现，如果已知结构，就可以推断出它的很多功能。反过来，如果知道了器官或组织的功能，也可推测其显微结构。

人体按结构和功能划分为四种基本组织：（1）上皮组织，覆盖在身体的表面或衬在体腔、管道内表面，还形成腺体。（2）结缔组织，连接、支持和保护身体各部分。（3）肌肉组织，收缩产生运动。（4）神经组织，产生并传递身体不同部位之间的神经冲动。

组织学是解剖学、生物化学和生理学的桥梁课。学习人体的显微结构可以帮助我们完成对大体解剖学的学习。生物化学研究生物体内的化学组成和化学变化过程。但化学分子，例如：酶、核酸、类脂等，并不是杂乱无章地在体内排列，而是在组成不同结构的细胞和组织中有规律地排列着。每种细胞、组织和器官都在执行着特定的功能。病理学研究疾病的病因和结果，以及由此引起的体内细胞、组织、器官所发生的结构和功能的变化。对正常组织结构的掌握是学习病理学的必要前提，不可能在对正常结构一无所知的情况下学习病理结构。虽然大多数医学生不会成为组织学家，但对组织学知识的熟练掌握，是他们将来成为医生的基础。

在所有生物学问题中，发生机制的研究最具挑战性。在基因控制下，从单细胞开始，到完整的多细胞器官的形成，以及接下来特定的生长和分化，这些过程在基因表达以前早已程序化了。在研究各种有机体的分化、发育及形态发生的各个发展阶段时，分子生物学、遗传学、生物物理学、生理学、免疫学和超微结构

分析技术等得到了应用。因此，研究人体发生的胚胎学与其他学科的关系也是愈来愈密切。

胚胎的早期发生过程是：受精和受精卵的形成，第三天桑椹胚的形成，植入后 5～7 天胚泡的形成，具有三胚层的胚盘在第三周形成。在胚胎发生发育过程中，一些有害因素可导致发育异常，最终可造成畸胎甚至死胎。所以，学习胚胎学对了解临床各科所见的先天性疾病是非常重要的。

对　话

1. 使用光镜的基本知识

教师： 光学显微镜是学习组织学的基本工具。在实验开始前，我们首先回忆一下显微镜的使用。显微镜摆在面前，如何正确移动它呢？请举手。请 Tony 同学回答一下。

Tony： 用右手握住显微镜镜臂。

教师： 这样就可以了吗？想一想，左手呢？（作手势提示）

Tony： 喔，知道了，应该同时用左手托住镜座。

教师： 对了，请坐。那么我们把标本放在什么位置呢？请 Alice 同学回答。

Alice： 放在载物台上。

教师： 不错，怎样移动标本呢？

Alice： 移动标本推进尺。

教师： 很好，请坐。请注意，我们这种显微镜不能用手直接移动标本。下面请打开显微镜光源，不要太亮。将标本放在载物台上，移动到物镜正下方，大家还知道哪个是物镜吧？

学生们： 知道。

教师： 好，下一步我们怎么将图像调节清晰呢？请 Tom 同学回答。

Tom： 旋转镜臂一侧的旋钮，升降载物台来调节图像。

教师： 正确，那些旋钮是粗准焦螺旋和细准焦螺旋。如果已经看到图像但不清晰，该怎么做？

Tom： 调节细准焦螺旋。

教师： 非常正确，很好，请坐。作为医学新生，为了把组织学学好，大家必须熟练掌握显微镜的使用。

2. 有关 HE 染色

教师： 请看电子图片，这属于哪种类型的标本呢？当然，是光学显微镜的。好，请 Alice 同学回答一下。

Alice： 是膀胱的石蜡切片标本。

教师： 对了，石蜡切片是最传统和常用的光镜切片技术。那么，石蜡切片常用的染色方法是那一种呢？

Alice： 苏木精－伊红染色。

教师： 简称 HE 染色，很好，请坐。HE 染色有什么特点呢？Bob 同学来试着回答一下，好吗？

Bob： 嗯……

教师： 不要紧张，别怕说错，请看图片中的细胞。

Bob： 喔，标本染成了蓝色和红色。

教师： 好，请仔细观察一下，细胞核是……

Bob： 细胞核染成了蓝紫色，细胞质红色。

教师： 非常好，请坐。染色可以增强标本的对比度，便于我们观察。掌握 HE 染色的特点有易于大家对细胞和组织的了解。

阅读材料

1. 干细胞生物工程

无论就其本身还是与治疗性基因转接相结合而言，组织工程与细胞疗法都具有能深深影响医学的潜能。以这些新进展为基础

的技术应用需要容易获得的细胞作为产生体外活细胞和组织的来源。由于其独具的终生重建机体功能性组织的能力，干细胞成为多种生物工程技术应用的颇具魅力的“原材料”。准确的说，通过分化为无数特殊的机能细胞，干细胞得以自我更新。目前的研究表明，干细胞存在于绝大多数组织中，而这些组织具有超出原来想象的变通力。尽管自干细胞生产细胞产品的潜能十分巨大，但目前尚无一套有效的体外培养干细胞或大批量刺激其分化成为功能性细胞的有效技术性方法。因此，从机制上掌握控制干细胞自我更新和细胞株系建立的条件十分重要，这对于指导体外干细胞及其衍生物培养生物过程的发展非常必要。

2. 中枢神经系统损伤后的干细胞修复

神经干细胞（NSCs）作为治疗一些中枢神经系统疾病的工具具有很大潜力。针对神经性疾病的治疗，无论是基础研究还是治疗新方法的建立，神经干细胞的广泛来源至关重要。NSCs 可以自胚胎或成体脑组织中分离，也可以由表达原癌基因的永生干细胞或小鼠与人的胚胎干细胞诱导产生。诱导形成的多种中枢和周围神经系统神经元细胞，以及少突胶质细胞、施旺细胞和星形胶质细胞，都由这些广泛来源的干细胞分化形成。

NSCs 在体外可通过许多途径增殖，同时保持其多向分化的潜力。植入成人中枢神经系统后，NSCs 主要分化为胶质细胞，但在起源于神经组织的区域除外。植入损伤或病变的成人中枢神经系统后，NSCs 的分化延迟。移植前和/或对受体环境改造前，体外调控 NSCs 对控制移植细胞的终末分化株系以获得大量功能性神经元是非常必要的。NSCs 和一些神经胶质细胞前体具有分化为少突胶质细胞和使中枢神经系统脱髓鞘轴突髓鞘再形成的能力。但这些通过移植获得再生的髓鞘功能有限。对于神经退行性疾病和中枢神经系统损伤而言，调控内源性神经前体可成为另外一种治疗方法或成为干细胞移植的辅助

疗法。然而，迄今为止这种方法尚未成功并且极具挑战性。了解中枢神经系统损伤后植入 NSCs 的分化机制对于获得这些治疗方法的成功是十分关键的。

3. 心脏组织工程：二维、三维（共）培养的协调收缩的新生大鼠肌细胞的特性

尽管采用了改良的缓解疗法，心脏病患者的预后仍然不良。心脏组织工程利用暂时的生物支架和心肌细胞，可能有助于为将来心脏疾病的治疗找到答案。为此，经过梯度细胞分离获得了两个新生大鼠的心室细胞片段。通过二维和三维细胞培养建立了具有时间相关特性的片段 I 和片段 II。在静态条件或在 HARV 生物反应器中培养，采用牛 I 型胶原基质构建了三维心脏结构。二维细胞培养条件下，1 天后收缩细胞出现且自第 5 天开始融合，可以持续到第 135 天。在片段 I 的收缩细胞（协调运动时）之间往往可以看到非收缩细胞。使用透射电子显微镜可以观察到这些主要的相关纤维原细胞。发现两个片段的 α－SM－1 肌动蛋白与肌钙蛋白－T 表达有所不同。两个片段中只是偶尔可以看到内皮细胞和巨噬细胞。贯穿整个三维基质，1～2 天后会出现悬垂式单细胞和细胞群收缩，导致这些细胞与胶原基质一起协调运动。整个过程片段 I 出现的比较快，可持续三周。三周后，肌钙蛋白－T 阳性细胞群散在分布于胶原基质中。而且，透射电子显微镜观察发现，胶原纤维之间有成层的以闰盘连接的健康的心肌细胞。这些发现为应用新生心肌细胞和纤维原细胞的共同培养物与胶原支架一起组成的可协调收缩的心肌细胞－基质结构的工程化提供了依据，这将为心肌层大面积创伤的修复带来希望。

（杨晓明　史玉兰）

Unit Four

Text

Physiology

For centuries, physiology and anatomy were the only recognized basic biomedical sciences. Recently, physiology and anatomy together with biology, chemistry, physics, psychology, and other sciences, have given rise to biomedical disciplines. Physiology may be distinguished from the other basic biomedical sciences by its concern with the function of the intact organism and its emphasis on the processes that control and regulate important properties of living systems.

Physiology is the study of biological function – of how the body works, from cell to tissue, tissue to organ, organ to system, and of how the organism as whole accomplishes particular tasks essential for life. The ultimate objective of physiological research is to understand the normal functioning of cells, organs, and systems.

In the healthy human, many variables are actively maintained within relatively narrow physiological limits. It includes body temperature, blood pressure, the ionic composition of blood plasma, blood glucose levels, the oxygen and carbon dioxide content of blood, and et al. The tendency to maintain the relative constancy of certain variables, even in the face of significant environmental change, is known as homeostasis. The concept of homeostasis has been of immense value in the study of physiology because it allows diverse regulatory mechanisms to be understood in terms of their "why" as well as their

"how" . The concept of homeostasis also provides a major foundation for medical diagnostic procedures. In order for internal constancy to be maintained, the body must have sensors that are able to detect deviations from a set point. The set point is analogous to the temperature set on a house thermostat. In a similar manner, there is a set point for body temperature, blood pressure, blood glucose levels and so on. When a sensor detects a deviation from a particular set point, it must relay this information to an integrating center, which usually receives information from many different sensors. The relative strengths of different sensory inputs are weighed in the integrating center, and, in response, the integrating center either increases or decreases the activity of particular effectors. Since the activity of the effectors is influenced by the effects they produce, and since this regulation is in a negative, or reverse direction, this type of control system is known as a negative feedback. In this way, constancy is maintained. Homeostasis is best conceived as a state of dynamic constancy, in which conditions are stabilized above and below the set point.

All of the information of physiology has been gained by application of the scientific method. The scientific method involves specific steps. In the first step, a hypothesis is formulated. In order for hypothesis to be scientific, it must be capable of being refuted by experiments or other observations of the natural world. Conclusions are then drawn as to whether the new data either refute or support the hypothesis. If the hypothesis survives such testing, it might be incorporated into more general theory. Scientific theories are statements about the natural world that incorporate a number of proven hypotheses. They serve as a logical framework by which these hypotheses can be interrelated and provide the basis for predictions that may as yet be untested.

New Words

psychology [sai'kɔledʒi] n. 心理学；心理状态
discipline ['disiplin] n. 学科；训练；纪律
organism ['ɔ: gənizəm] n. 生物；有机体；组织
variable ['vɛəriəbl] n. 变数；变量 adj. 变化的,易变的,可变的
homeostasis [ˌhəumiəu'steisis] n. 内稳定，动态平衡
sensor ['sensə] n. 感受器；传感器；敏感元件
thermostat ['θə:məstæt] n. 恒温器
effector [i'fektə] n. 效应器
formulate ['fɔ:mjuleit] vt. 明确地叙述;用公式表示;按配方制造
refute [ri'fju:t] vt. 驳斥，驳倒，反驳，证明（某人）看法不对
hypothesis [hai'pɔθisis] n. 假设；假说；前提
incorporate [in'kɔ:pəreit] vt. 合并；组成公司；具体表现
prediction [pri'dikʃən] n. 预计；预测；预言；预报

Phrases and Expressions

body temperature　体温
blood pressure　血压
ionic composition　离子组成
blood plasma　血浆
blood glucose　血糖
carbon dioxide　二氧化碳
set point　调定点
integrating center　整合中枢
negative feedback　负反馈
dynamic constancy　动态平衡

Questions

1. What does the physiology aim at?

2. How to understand the term of homeostasis?
3. How does the integrating center work to maintain the dynamic constancy of body?
4. What is the scientific method in biomedical sciences?
5. Make a speech or write a summary about the text.

Dialogue

1. Discuss Experiment Result

Teacher : Ok, then, now that our experiment of identifying blood type went on smoothly, it's time for us to discuss our results.

Students : Yes, we're ready.

Teacher : If the agglutination happened on the side of A agglutinin, but not on the B agglutinin, what the blood type should be?

Students : It's blood type A.

Teacher : Well, if the agglutination happened on the side of B agglutinin, but not on the A agglutinin, what's the blood type?

Students : It's blood type B.

Teacher : If the agglutination happened on the both sides, then what 's the result?

Students : It's blood type AB.

Teacher : If the agglutination happened on the neither side, what is it?

Students : It's blood type O.

Teacher : Excellent.

2. In the Classroom

Teacher : Good morning, everyone.

Students : Good morning, teacher.

Teacher : Before we begin our class, let's review what we learned in last class. I'll make some students answer my questions.

Students : Ok.

Teacher : Roy, can you tell us how the body regulates himself?

Roy : The body regulates by three pathways, they are nervous regulation, humoral regulation and auto – regulation.

Teacher : All right, sit down please. Henry, do you know what the three levels are regarding to the research of physiology?

Henry : They are cell or molecular level, organ or system level and the whole body level.

Teacher : Well, the next question is how many parts body fluid is divided into? David, can you?

David : The body fluid is divided into two parts. They are intracellular fluid and extracellular fluid.

Teacher : Great.

Reading Material

1. Synapses and Neurexins

At the junction between two neurons, the machinery that releases neurotransmitter from one cell must lie near calcium and align with detectors in the receiving cell. The computational power of the brain depends on the precise connections, or synapses, that link together the many billions of nerve cells. Specialized to allow rapid

(millisecond) neuronal communication, synapses work broadly as followed. In response to an electrical impulse, the terminal of a 'presynaptic' neuron releases chemical neurotransmitters, which diffuse across the synaptic cleft to activate specific receptors on the postsynaptic neuron. These receptors cause an electrical discharge in the postsynaptic cell, thereby propagating the electrical signal.

It has been known that electrical impulses propagating down a neuron cause an influx of calcium ions through votage – gated calcium channels; this in turn triggers neurotransmitter release. The rapidity with which calcium influx leads to neurotransmitter release (within 200 microseconds) means that the voltage – gated calcium channels must be very close to – perhaps even opposite cluster of neurotransmitter receptors in the postsynaptic membrane. An attractive idea is that this alignment is achieved by adhesion molecules – specific cell – surface proteins located on both sides of the synapse that grip each other across the synaptic cleft and hold the presynaptic and postsynaptic apparatuses in register.

One family of cell – surface proteins implicated in synapse formation and adhesion is the neurexins. Originally identified by their binding to α – latrotoxin (a spider toxin that triggers neurotransmitter release), the neurexins are presynaptic transmembrane proteins that have a large extracellular region and a short intracellular tail. A striking feature of neurexins is their molecular diversity: they are encoded by three genes each of which has two regulatory regions; this means that long (α) and short (β) neurexin proteins can be generated from each gene. In addition, the messenger RNAs encoded by each gene can be processed in different ways (by 'alternative splicing'), resulting in thousands of distinct protein forms.

Because of their great diversity and their presence on the surface

of presynaptic terminals, neurexins became attractive candidates for determining the specificity of synaptic connections. Consistent with this idea, specific neurexin proteins bind through their extracellular domain to neuroligins, a family of transmemebrane receptors found in the postsynaptic memebrane, and to dystroglycan, a cell - surface protein of unknown function in the brain. The interaction of neuroligin and neurexin in cultured neurons induces morphological events resembling synapse formation, implying that neurexins function in the specification and initiation of synapse formation. The intracellular tails of neurexin and neuroligin bind respectively to CASK and PSD - 95, two proteins that are believed to organize additional proteins of the presynaptic and postsynaptic membranes and link them to the neuron's internal skeleton (the cytoskeleton) . This series of protein interactions could enable a neurexin - neuroligin compex to glue together presynaptic and postsynaptic elements.

2. The Red Blood Corpuscles

Red blood corpuscles are biconcave discs with a thickness at the edge of about 2μm and a diameter of 7 μm. They have no nucleus. In a drop of fresh blood, the red corpuscles resemble a heap of coins. Red corpuscles consist of a stroma or framework containing mainly water (about 60 per cent) and haemoglobin (30 per cent) which consists of an iron - containing pigment (haem) combined with a protein (globin) . The main property of haemoglobin is its ability to form a loose compound with oxygen, although it also plays a part in regulating the acid - base balance of the blood and the carriage of carbon dioxide. The main function of the red corpuscles is the carriage of oxygen from the lungs to the tissues.

There are about 5 million red corpuscles per cubic mm of blood in men and about 4. 5 million per cubic mm in women. Red corpuscles are formed in the red bone marrow of the bones of the skeleton (mainly in the flat bones and bodies of the vertebrae) and after a life of about 110 days they are broken down in the spleen. The iron is stored in the liver and used again, and the pigments are used by the liver to form the bile pigments.

Several substances are required for the formation of a sufficient number of normal red corpuscles – protein, iron, vitamin C, vitamin B12 (extrinsic factor), folic acid and an intrinsic factor, formed by the lining of the stomach. Liver contains both folic acid and the extrinsic and intrinsic factors. A common form of anaemia is due to lack of iron (simple anaemia). In this type, the number of red corpuscles is fairly normal but the amount of haemoglobin in each corpuscle is reduced. The administration of iron can cure this form of anaemia. Another type of anaemia is called pernicious anaemia in which the number of red corpuscles is less than normal. This is much less common and is due to a lack of intrinsic and extrinsic factors, and the administration of liver will cure it.

3. Umbilical Cord Tissue – Derived Neural Transplantation

To investigate the neural differentiating capability of the umbilical cord tissue – derived stromal cells (UCSCs) in the attempt to find a new cell source for neural transplantation. UCSCs from umbilical cord of human were cultured with tissue piece method, passaged by trypsin digestion. Cells were identified with immunocytochemistry. Stromal cells that migrated from explants and primary culture were obtained.

These cells could differentiate into smooth muscle cells spontaneously and expressed smooth muscle actin; Salvia miltiorrhiza could induce these cells to differentiate into the neuron - like cells, which displayed typical neuron morphology, expressed nestin, β - tubulin and neurone specific enolase (NSE) at the early stage of differentiation, and were stained by anti - neurofilament 200 at the late stage of differentiation. With optimal conditions, about 90% of UCSCs expressed neuronal phenotypes, lower than 1% of the differentiated cells expressed GFAP, and no myelin basic protein expression was detected in the differentiated cells, indicating the absence of oligodendrocyte differentiation from stromal cells. The data supported the hypothesis that the umbilical stem cells with the ability of differentiating into neurons, which may provide an native stem cell source for central nervous system cell transplantation.

参考译文

课　文

生理学

几个世纪以来，仅生理学和解剖学被认为是生物医学的基础学科。近年来，生理学和解剖学与生物学、化学、物理、心理学及其他一些学科一起促进了生物医学学科的发展。生理学与其他基础生物医学学科的区别在于，它研究的是整个机体的功能，尤其是生命重要体征的控制和调节过程。

生理学是研究生物机体功能的科学，包括从细胞到组织，从组织到器官，从器官到系统，人体是如何运转工作的，以及整个机体是如何完成生命所必需的特定功能的。生理学研究的最终目的是了解细胞、器官和系统的正常功能。

健康人体中有许多生理指标都维持在比较狭窄的生理范围内，包括体温、血压、血浆中离子组成成分、血糖水平、血液中氧气和二氧化碳含量等。即使环境发生明显变化时，这些生理指标仍能保持相对恒定，这就是内稳定。在生理学的研究中，内稳定的概念非常重要，因为其中存在着的不同调节机制解释了机体“为什么”以及“如何”变化。内稳定的概念也为医学诊断过程提供了重要基础。为了维持机体内部生理平衡，机体必须有能够监控偏离调定点的感受器，调定点类似房屋恒温器中的温度调定设备。同样的，机体也存在体温、血压、血糖水平等的调定点。当感受器感受到某项生理指标偏离调定点时，就能将此信息传入整合中枢，整合中枢接受来自不同感受器的信息，不同感受器传入信息的相对强度在整合中枢加以分析整合，整合中枢就能增强或减弱特定效应器的活动。由于效应器的活动是受自身所产生效应的影响，而且这种调节是负向或反向的，所以这种控制系统被称为负反馈。这样，某种生理平衡就得以维持。内稳定最好被认为是一种动态平衡，在这种条件下，生理水平可以维持在调定点左右。

生理学的所有内容均是应用科学方法得来的。科学方法包含特定的步骤。第一步先形成假设。为了证明假设是科学的，必须经受来自试验或其他对自然界观察的批驳。根据新的实验数据反驳还是支持这一假设从而得出结论。如果试验证明假设是正确的，这一假设会被具体化形成普遍的理论。自然界的科学理论都是由许多已被证明的假设总结得来的，它们形成了一个逻辑框架，通过这一框架许多假设相互联系，并且为未知预言提供了基础。

对　话

1. 讨论实验结果

教师： 好了，我们的血型鉴定实验做得很顺利，现在我们讨论一下实验结果。

学生： 我们准备好了。

教师： 如果 A 侧血清发生了凝集反应而 B 侧没有发生，这应该是什么血型？

学生： 是 A 型。

教师： 那么，如果 B 侧血清发生了凝集反应而 A 侧没有发生，这又是什么血型？

学生： 是 B 型。

教师： 如果两侧均发生凝集反应，结果是什么？

学生： 是 AB 型。

教师： 如果两侧均没有发生凝集反应，血型是什么？

学生： 是 O 型。

教师： 好极了。

2. 在教室

教师： 同学们，早上好。

学生： 老师好。

教师： 在进行新的内容之前，我们先复习一下上次课学过的内容。下面我提几个问题。

学生： 好的。

教师： Roy，你能给我们说一下机体是怎样调节自身的吗？

Roy： 机体调节可通过三种方式，分别是神经调节、体液调节和自身调节。

教师： 很好，请坐。Henry，你知道生理学的三个研究水平吗？

Henry： 它们是细胞分子水平、器官系统水平和整体水平。

教师： 下一个问题是体液分成几部分，David，你能告诉大家吗？

David： 体液分成两部分，即细胞内液和细胞外液。

教师： 非常好。

阅读材料

1. 突触与神经细胞素蛋白质

在两个神经元的连结处，神经递质的释放必须在钙通道附近，并与接收神经元的感受器之间建立联系。脑的计算能力依靠能把好几十亿的神经元结合在一起的准确的神经连接，即突触。为了达到快速（毫秒）的神经元联系，神经突触的作用非常广泛。针对电冲动，突触前神经元的终端释放特定的化学神经递质，它可穿过突触间隙，使突触后神经元上的特殊感受器活化。这些感受器可使突触后神经元细胞发生电位变化，进而产生电信号。

已知神经冲动向下一个神经元传导可导致突触前膜的电压门控钙通道开放，引起钙离子的流入，进而诱发神经递质的释放。钙流入诱发神经递质释放的速度（200 微秒内）极快，这意味着电压门控的钙通道必然非常接近甚至就在突触后膜神经递质感受器的对面。有趣的是，这种将突触前、后结构和突触间隙连成一体的特定联合，是由位于突触双侧的细胞表面特殊蛋白质－粘附分子完成的。

使神经突触形成和粘附的一个细胞表面蛋白质家族是神经细胞素。最初按照它们是否能与 α－毒蛛素（一种能诱发神经递质释放的蜘蛛毒素）结合而分类。神经细胞素是突触前膜上的跨膜蛋白质，它有较大的胞外区和短的胞内区末端。神经细胞素的一个显著特点是其分子多样性：它们由 3 个基因编码，而各自又有 2 个调节区。也就是说，每个基因都能产生长（α）和短（β）神经细胞素蛋白质。另外，每个基因的 mRNAs 在不同的方式下（任意剪切）编码，可产生数以千计的不同蛋白质。

由于存在着多样性，以及这些多样性蛋白存在于突触前膜末端的表面，神经细胞素成为决定突触连接特异性的重要因素。与之相对应，特定的神经细胞素蛋白质通过它们的细胞外决定区与 neuroligin（一种位于突触后膜的跨膜蛋白受体家族）结合，同

时也与 dystroglycan（一种功能不明的存在于脑部的细胞表面蛋白）结合。在培养的神经元中，neuroligin 和神经细胞素的相互作用可诱导神经突触形态上的修复形成，提示我们，neuroligin 在突触形成的种类和始动中发挥作用。神经细胞素和 neuroligin 的胞内区末端分别与突触前后膜的两种其他组成蛋白 CASK 和 PSD－95 结合，可使它们与神经元内部骨架（细胞骨架）连在一起。这一系列的蛋白质相互作用使得通过神经细胞素－neuroligin 复合体将突触前后成分粘合在一起。

2. 红细胞

红细胞是两面凹的盘状物，其边缘厚约 2μm，直径约 7μm，没有细胞核。在一滴鲜血中，红细胞的排列就象一沓硬币。红细胞含有一种基质或骨架结构，主要由水（约 60%）和血红蛋白（30%）组成，血红蛋白由一种含铁的色素（血红素）和一种蛋白质（珠蛋白）结合而成。血红蛋白的主要特性是，虽然它在血液酸碱平衡的调节中也起到部份作用，并能携带二氧化碳，但它也能与氧形成一种松散的化合物。红细胞的主要功能是将氧由肺运送到组织。

每立方毫米的血液中，男子约有 500 万个红细胞，女子约为 450 万个。红细胞在骨骼（主要在扁骨和椎骨体内）的红骨髓中产生，大致经过 110 天后，它们在脾脏中被分解。铁质储藏于肝脏并可再利用，而色素则被肝脏用来形成胆色素。

要形成足够数量的正常红细胞，有些物质是必需的，如蛋白质、铁、维生素 C、维生素 B_{12}（外源性因子）、叶酸和一种由胃粘膜产生的内源性因子。肝脏中既含有叶酸也含有内、外源性因子。常见的贫血是由于铁质缺乏（单纯性贫血）。在这种类型的贫血中，红细胞的数目相当正常，而每个红细胞内的血红蛋白减少，补充铁剂能治疗这类贫血。另一种贫血称为恶性贫血，在这种情况下，红细胞的数目低于正常，这种贫血非常少见，是由

内、外源性因子缺乏引起的，可采用肝制剂治疗。

3. 脐带组织来源的神经移植

研究人脐带组织来源的基质细胞（UCSCs）向神经细胞分化的能力，是为神经移植探寻新的细胞来源。采用组织块法培养UCSCs，酶消化法对细胞进行传代，应用免疫细胞化学的方法对细胞进行鉴定，获得来自移植物和原代培养的基质细胞。这些细胞可自发分化为平滑肌细胞，并表达平滑肌肌动蛋白。丹参注射液可诱导其分化成为具有典型神经细胞形态的神经元样细胞，早期分化阶段可表达巢蛋白、β－微管蛋白和神经元特异性烯醇化酶（NSE），后期分化阶段可表达神经微丝200 。在合适的诱导条件下，大约90 % 的 UCSCs 可表达神经元细胞的表型，低于1% 的分化细胞可表达 GFAP（代表星型胶质细胞），无髓鞘基础蛋白的表达，说明无少突胶质细胞分化形成。这些数据支持脐带干细胞可分化成为神经元细胞的假说，脐带干细胞可为中枢神经系统细胞移植提供自身干细胞来源。

（耿进霞）

Unit Five

Text

Biochemistry

Biochemistry is the science concerned with the various molecules that occur in living cells and organisms and with their chemical reaction. Biochemistry can be defined more formally as the science concerned with the chemical basis of life.

The major objective of biochemistry is the complete understanding at the molecular level of all of the chemical processes associated with living cells. To achieve this objective, biochemists have sought to isolate the numerous molecules found in cells, determine their structures, and analyze how they function. To give one example, the efforts of many biochemists to understand the molecular basis of contractility with muscle cells have entailed purification of many molecules, both simple and complex, followed by detailed structure – function studies. Through these efforts, some of the features of the molecular basis of muscle contraction have been revealed. A further objective of biochemistry is to attempt to understand how life began. Knowledge of this fascinating subject is still embryonic.

The scope of biochemistry is as wide as life itself. Wherever there is life, chemical processes are occurring. Biochemists study the chemical processes that occur in microorganisms, plant, insects, fish, birds, mammals, and human beings. Students in the bio – medical sciences will be particularly interested in the biochemistry of the two latter groups. However, an appreciation of the biochemistry of less complex forms of life is often of direct relevance to human biochemistry. For instance, contemporary theories on the regulation of the activities of genes and of enzymes in humans emanate from pioneering studies on bread molds and on bacteria. The field of recombinant DNA emerged from studies on bacteria and viruses; their rapid multiplication times and the ease of extracting their genetic material make them suitable for genetic analyses and manipulations. Knowledge gained from the study of viral genes responsible for certain types of cancer in animals (viral oncogenes) has provided profound insights into how human cells become cancerous.

The knowledge of biochemistry is essential to all life sciences.

The biochemistry of the nucleic acids lies at the heart of genetics; in turn, the use of genetic approaches has been critical for elucidating many areas of biochemistry. Physiology, the study of body function, overlaps with biochemistry almost completely. Immunology employs numerous biochemical techniques, and many immunologic approaches have found wide use by biochemists. Pharmacology and pharmacy rest on a sound knowledge of biochemistry and physiology; in particular, most drugs are metabolized by enzyme – catalyzed reactions, and the complex interactions among drugs are understood best biochemically. Poisons act on biochemical reactions or processes; this is the subject matter of toxicology. Biochemical approaches are being used increasingly to study basic aspects of pathology (the study of disease), such as inflammation, cell injury, and cancer. Many workers in microbiology, zoology, and botany employ biochemical approaches almost exclusively. These relationships are not surprising, because life as we know it depends on biochemical reactions and processes. In fact, the old barriers among the life sciences are breaking down, and biochemistry is increasingly becoming their common language.

Medical students who acquire a sound knowledge of biochemistry will be in a strong position to deal with two central concerns of the health sciences: (1) the understanding and maintenance of health and (2) the understanding and effective treatment of disease. Biochemistry impacts enormously on both of these fundamental concerns of medicine. In fact, the interrelationship of biochemistry and medicine is a wide, two – way street. Biochemical studies have illuminated many aspects of health and disease, and conversely, the study of various aspects of health and disease has opened up new areas of biochemistry. For instance, the knowledge of protein structure and

function was necessary to elucidate the single biochemical difference between normal and sickle cell hemoglobin. On the other hand, analysis of sickle cell hemoglobin has contributed significantly to our understanding of the structure and function of both normal hemoglobin and other proteins.

This relationship between medicine and biochemistry has important philosophical implications for the former. As long as the medical treatments are firmly grounded on knowledges of biochemistry and other relevant basic sciences (eg. physiology, microbiology, nutrition), the practice of medicine will have a rational basis that can be adapted to accommodate new knowledge. Biochemical approaches are often fundamental in illuminating the causes of diseases and in designing appropriate therapies. The judicious use of various biochemical laboratory tests is an integral component of diagnosis and monitoring of treatment.

New Words

biochemistry ['baiəu'kemistri] n. 生物化学
contractility [kɔn'træktiliti] n. 收缩
purification [ˌpjuərifi'keiʃən] n. 净化，纯化
fascinating ['fæsineitiŋ] adj. 迷人的，醉人的，着魔的
embryonic [ˌembri'ɔnik] adj. 胚胎的
mammal ['mæməl] n. 哺乳动物
contemporary [kən'tempərəri] adj. 当代的，同时代的
n. 同时代的人
emanate ['emәneit] vi. 散发，发出，发源
mold [məuld] n. 霉，霉菌
bacteria [bæk'tiəriə] n. 细菌
virus ['vaiərəs] n. 病毒

multiplication [ˌmʌltipli'keiʃən] n. （动、植物的）繁殖，增殖
genetic [dʒi'netik] adj. 遗传的，起源的
viral ['vairəl] adj. 病毒的
elucidate [i'lju:sideit] vt. 阐明，说明
overlap ['əuvə'læp] v. （与……）交迭
immunology [ˌimju'nɔlədʒi] n. 免疫学
pharmacology [ˌfa:mə'kɔlədʒi] n. 药理学
pharmacy ['fa:məsi] n. 药剂学，药房，配药业，制药业
enzyme ['enzaim] n. 酶
catalyze ['kætəlaiz] vt. 催化，刺激，促进
toxicology [ˌtɔksi'kɔlədʒi] n. 毒物学
pathology [pə'θɔlədʒi] n. 病理学
botany ['bɔtəni] n. 植物学
exclusively [ik'sklu:sivli] adv. 全部地，完全地，排外地，专有地
illuminate [i'lju:mineit] vt. 阐明，说明
hemoglobin [ˌhi:məu'gləubin] n. 血红蛋白
philosophical [ˌfilə'sɔfikəl] adj. 哲学的
judicious [dʒu (:)'diʃəs] adj. 明智的

Phrases and Expressions

be concerned with　有关
chemical reaction　化学反应
be defined as　被定义为，被确定为
viral oncogene　病毒原癌基因
impact on　对……产生影响
sickle cell hemoglobin　镰刀状细胞血红蛋白

Questions

1. Are there any professional relationships between biochemistry and physiology?
2. Why should we study the single forms of life when we want to understand the biochemistry of human being?
3. Please describe the main scope of biochemistry.
4. What is oncogenes?
5. Make a speech or write a summary about the text.

Dialogue

About Alzheimer Disease

George : Do you know something about Alzheimer disease?

Cissy : Just a little. It seems to be an incurable neuropsychiatric condition in which progressive impairment of cognitive function occurs, usually accompanied by affective and behavioral disturbances.

George : Yeah. I am reading some materials about this kind of disease.

Cissy : Oh! Read for me, please.

George : About 2 million people in the USA suffer from Alzheimer disease, and its prevalence is likely to increase as more people live longer. Some cases have a familial basis, but the majority appears to be sporadic.

Cissy : Can Alzheimer disease lead to dementia?

George : Yes, Alzheimer disease is the commonest cause of dementia. It can be defined as a progressive decline in intellectual functions, due to an organic cause, that interferes substantially with an individual's activities. The usual age at onset is

over 65 years, but the disease can appear in the early 40s; survival ranges from 2 to 20 years. Loss of memory is often the first sign. The disease usually progresses inexorably, and terminal patients are completely incapacitated.

Cissy : Terrible disease! Why is it to be?

George : The actual mechanism of Alzheimer disease is still not clear. Someone thought that genetic gene mutant leads to amyloid deposition. There are other hypotheses concerning the causation of Alzheimer disease. For instance, it has been proposed that it may be caused by infection with a slow virus, though no such virus has been isolated with any consistency. Someone suggested that ingestion of elevated amounts of aluminum may cause Alzheimer disease.

Cissy : Is no specific drug therapy available for Alzheimer disease because of its unclear causes?

George : No, specific drug is not available.

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Reading Material

1. Lens Superoxide Dismutase and Catalase Activities in Diabetic Cataract?

Biochemical evidence suggests that the oxidative damage of the lens proteins is involved in the genesis of senile cataract and the development of diabetes – related pathology changes such as the formation of cataracts. In particular, lens proteins are subject to extensive oxidative modification. Oxidative damage either decreases the antioxidant capacity or decreased antioxidant capacity results in

oxidative damage. The purpose of this study was to analyze the activities of the antioxidant enzymes such as Cu, Zn Superoxide Dismutase (Cu, Zn – SOD) and catalase in the cataractous lenses of the type 2 diabetic group and cataractous lenses of the senile group, so eighteen diabetic cataractous lenses and twenty six senile cataractous lenses were studied. Cu, Zn – SOD activity was measured in lenses by enzymatic method and catalase activity was measured by Goth's colorimetric method.

Results showed that Cu, Zn – SOD levels were significantly lower in the diabetic cataractous lenses than senile cataractous lenses (8.052 ± 0.818 mg/g, 18.216 ± 4.217mg/g, $P < 0.05$). Similarly, catalase levels were significantly lower in the diabetic cataractous lenses than senile cataractous lenses (0.326 ± 0.134kU/g, 0.665 ± 0.322kU/g, $P < 0.001$). The results of the present study indicate that the antioxidant capacity in the diabetic cataractous lenses was decreased and this result suggests a role of antioxidant enzymes in the genesis of diabetic cataracts.

2. Ultrasensitive Immunoassay and Determination of Pregnancy Associated Plasma Protein – A in Coronary Heart Disease

Markers of myocardial injury have been vital in the assessment of patients with coronary heart disease. Pregnancy associated plasma protein A (PAPP) – A is an insulin – like growth factor (IGF) binding protein (IGFBP) – 4 protease and a potential early indicator of unstable angina. We developed an ultrasensitive enzyme – linked immunosorbent assay (ELISA) for PAPP – A and measured serum

PAPP – A in patients with biochemical evidence of acute coronary syndrome.

Method development was based on pair – wise evaluation of a panel of antibodies and determination of PAPP – A specificity and sensitivity relative to those of a conventional method. Association of PAPP – A with myocardial damage was assessed in serum samples classified based on serum creatine kinase (CK) – MB or cardiac troponin – T levels. Results showed, serum PAPP – A was significantly higher in samples with elevated CK – MB or troponin – T than in samples with normal CK – MB ($P < 0.001$). Marker – association studies showed strong correlation between PAPP – A and troponin – T ($r = 0.59, P < 0.001$) in a subset of troponin – T positive samples. Indications for both parallel as well as divergence in the expression of PAPP – A and troponin – T were also evident when serial timed samples available from a number of patients were analyzed.

The data are consistent with the conclusion that expression of PAPP – A is enhanced in patients with biochemical evidence of acute coronary syndrome and suggest strongly that demonstration of PAPP – A association with other cardiac markers might be influenced by their relative release dynamics (timing and duration). The availability of the ultrasensitive PAPP – A ELISA should facilitate systematic investigations of PAPP – A expression in this and other pathophysiological conditions that might involve altered expression of the IGF/PAPP – A system.

3. Deposition of Amyloid β Protein in Brain and Alzheimer Disease

The basic pathologic picture of Alzheimer disease is of a degenerative

process characterized by the loss of cells in certain areas of the brain (eg. the cortex and hippocampus) . At the microscopic level, amyloid plaques surrounded by nerve cells containmg neurofibrillary tangles (paired helical filaments formed from a hyperphosphorylated form of the microtubule associated protein, tau) are hallmarks. Deposits of amyloid are frequent in small blood vessels.

Intensive research is under way to determine the cause of Alzheimer disease. Significant progress has been made recently. Particular interest has focused on the presence of amyloid β peptide (Aβ), the major constituent of the plaques found in Alzheimer disease. The amyloid cascade hypothesis holds that deposition of Aβ is the cause of the pathologic changes observed in the brains of victims of Alzheimer disease and that of other changes, such as neurofibrillary tangles and vascular alterations, are secondary. Aβ is derived from a larger precursor protein named amyloid precursor protein (APP), whose gene is located on chromosome 21 close to the area affected in Down syndrome (trisomy 21) . Individuals with Down syndrome who survive to age 50 often suffer from Alzheimer disease.

APP is a transmembrane protein that can exist as different isoforms. The Aβ peptide can vary in length from about 39 ~ 42 amino acids, with the latter being most amyloidogenic. When split off from its parent protein, Aβ forms an insoluble extracellular deposit. APP can be cleaved by at least three enzymes, α - secretase produces a soluble fragment (sAPPα) containing only part of Aβ. The actions of β and γ secretase split off Aβ from APP. How these enzymes are regulated is still to be established. There is evidence that exposure of neurons to Aβ can increase their intracellular concentration of Ca^{2+} . Some protein kinases, including that involved in phosphorylation of tau, are regulated by levels of Ca^{2+} . Thus, increase of tau and

formation of the paired helical filaments present in the neurofibrillary tangles.

Certain cases of Alzheimer disease are known to have a familial basis. The finding of mutations in the gene on chromosome 21 encoding APP caused great excitement, as it seemed a likely candidate for involvement in most cases of Alzheimer disease. However, this gene appears to be involved in only a small number of cases. Two other genes have been isolated that are involved in certain familial cases of Alzheimer disease. They appear to encode transmembrane proteins, which show homology to the SPE -4 protein of Caenorhabditis elegans, a roundworm whose genome has now been sequenced in relation to the Human Genome Project. This protein appears to be involved in the transport of soluble and membrane - bound proteins. This has led to speculation that the proteins (aptly named "presenilins") encoded by the newly discovered genes may participate in transport or processing of APP.

At present, a definitive diagnosis of Alzheimer disease can often be made only by finding the characteristic plaques at autopsy. No specific drug therapy for Alzheimer disease is available. Brain - derived nerve growth factor has been shown to be deficient in certain areas of the brains of patients with Alzheimer disease, and its possible therapeutic benefit is being studied in animals.

To summarize, while amyloid plays a central role in Alzheimer disease, it is not yet clear whether in great majority of cases its deposition is a primary event or whether it occurs secondary to various other biochemical phenomena. The recent discovery of mutations in genes at first glance unrelated to amyloid deposition has opened up new pathways of research that might lead to a more complete understanding of the mechanisms responsible for this tragic disease.

参考译文

课　文

生物化学

生物化学是研究细胞和有机体内各种分子及其化学变化的科学。进一步说，生物化学也就是研究生命化学的科学。

生物化学研究的主要目的是在分子水平上全面了解与活细胞有关的所有化学过程。为了达到此目的，生物化学家尝试着分离细胞中所发现的众多分子，测定其结构，分析它们如何发挥作用。例如，为了理解肌细胞收缩的分子基础，许多生物化学家共同努力，对许多简单和复杂的分子进行了纯化，并详细研究其结构功能。经过努力，最终揭示了肌肉收缩分子基础的一些特征。生物化学研究的另一目的是试图了解生命是如何起源的。人们对这个引人注目的课题的认识仍仅局限于胚胎方面的知识。

生物化学研究的范围正如生命本身一样宽广，哪里有生命，哪里就会出现化学反应。生物化学家研究发生在微生物、植物、昆虫、鱼、鸟、哺乳动物和人体内的化学过程，学习生物医学的学生对生物化学研究的后二者尤其感兴趣。然而，对简单生命的生物化学评价常常直接与人类生物化学相关。例如，当代有关人类基因和酶活性调控的理论就来自于对面包霉变和细菌的早期研究。重组 DNA 技术领域就是从对细菌和病毒的研究开始的；细菌和病毒繁殖迅速、遗传物质易于提取的特点使其适于进行遗传学分析和操作。对动物某些癌变病毒基因（病毒原癌基因）的研究所获得的知识，为研究人体细胞如何发生癌变开辟了宽广的视野。

生物化学知识对所有生命科学都是必需的。核酸的生物化学处于遗传学的核心位置，而遗传学方法的应用对于阐明许多生物

化学领域是非常关键的。生理学是对人体功能的研究，几乎完全与生物化学交叉迭连。免疫学采用了大量生物化学技术，许多免疫学方法又被生物化学家广泛应用。药理学和药剂学要以相当坚实的生化及生理知识为基础，特别是大多数药物需经过酶的催化作用进行分解代谢，且药物间复杂的相互作用需要生物化学知识才能更好地得以解释。毒物对生物化学反应或过程起作用，这是毒理学研究的范畴。生物化学方法越来越多地被应用于病理学（对疾病的研究），如炎症、细胞损伤和癌症。许多研究微生物、动物学和植物学的工作者几乎完全应用生物化学方法。这些联系并不足以为奇，因为正如我们所知的，生命依赖于生物化学反应和过程。事实上，生命科学中的旧障碍正在被破除，而生物化学逐渐成为生命科学的共同语言。

获得了相当坚实的生物化学知识的医学生将在解决卫生科学的两个中心问题时占重要地位：（1）对健康的了解和维护；（2）对疾病的了解和有效治疗。生物化学在很大程度上影响着医学的这两大基本问题。事实上，生物化学与医学的相互关系是广泛且双向的。生物化学研究阐明了健康和疾病许多方面的问题，相反，对健康和疾病各个方面的研究又为生物化学开辟了新领域。例如，蛋白质结构与功能方面的知识对解释正常与镰刀状细胞血红蛋白间单一生物化学差异是必需的。另一方面，分析镰刀状细胞血红蛋白十分有助于我们了解正常血红蛋白和其他蛋白质的结构和功能。

医学与生物化学的这种关系对前者有着重要的哲学含义。只要医学治疗牢固建立在生物化学和其他相关基础学科（例如：生理学、微生物学、营养学）知识基础之上，那么医学实践将有一个适当的基础以适应新认识的积累综合。生物化学方法常常是阐明病因及确定恰当治疗方案的基础，各种生物化学实验方法的合理利用是诊断和指导治疗的组成部分。

对　话

有关 Alzheimer 病

George：你知道 Alzheimer 病吗?

Cissy：略知一二。它好像是一种无法治愈的进行性认知功能受损的神经精神疾病，常伴有情感和行为障碍。

George：对。我正在看有关这种疾病的一些资料。

Cissy：喔，念给我听听吧。

George：在美国，约有 2 百万人患有 Alzheimer 病，且随着寿命较长的人越来越多，发病率似乎也在增高。一些病例有家族遗传基础，但是大多数病例似乎是散发的。

Cissy：Alzheimer 病能引起痴呆吗?

George：是的，Alzheimer 病是引起痴呆最常见的原因，它被认为是由于器官原因而干扰了人体活动所引起的进行性智能下降。通常的发病年龄是在 65 岁以后，但也可能出现在 40 多岁；生存期从 2 年到 20 年不等。记忆缺失常常是首发症状，通常呈不可逆进行性发展，最终病人完全残疾。

Cissy：好可怕的病！为什么会这样呢?

George：确切病因还不清楚。有人认为是遗传性基因突变引起淀粉样蛋白沉积所致。还有一些有关病因的假说，例如有人提出它可能是由于感染了慢病毒引起的，尽管这种病毒还未在任何病例中分离出来。有人认为是由于铝摄取量增加而引起的。

Cissy：既然病因不清楚，那治疗也没有什么特效药吧?

George：是的，没有特效药物可用。

……

阅读材料

1. 糖尿病性白内障患者晶体中 SOD 和过氧化氢酶活性的测定

生化证据表明，晶体蛋白的氧化损伤与老年性白内障的形成及糖尿病相关病理变化（例如：白内障的形成）的发展有关。特别是，大量的氧化修饰可限制晶体蛋白功能的正常发挥，氧化损伤可降低机体的抗氧化能力，而机体抗氧化能力的降低又可导致氧化损伤。为了研究Ⅱ型糖尿病性白内障和老年性白内障患者晶体中抗氧化酶（例如：Cu、Zn－SOD 和过氧化氢酶）的活性，我们对 18 例糖尿病性白内障和 26 例老年性白内障患者的术后晶体，采用黄嘌呤氧化酶系统测定法分析 Cu、Zn－SOD 活性，Goth's 比色法测定过氧化氢酶活性。

结果显示，Ⅱ型糖尿病性白内障患者晶体 Cu、Zn－SOD 活性明显低于老年性白内障患者（分别为每克蛋白 8.052 ± 0.818mg，18.216 ± 4.21mg，$P<0.05$）。同样，Ⅱ型糖尿病性白内障患者的过氧化氢酶活性也明显低于老年性白内障患者（分别为每克蛋白 0.326 ± 0.134kU，0.665 ± 0.322kU，$P<0.001$）。目前的实验结果表明，糖尿病性白内障患者晶体中抗氧化活性降低，因此推测，抗氧化酶在糖尿病性白内障的发生中起着一定的作用。

2. 超敏感免疫法及其对冠心病患者妊娠相关性血浆蛋白 A 的检测

心肌损伤的标志物在对冠心病患者的评估中很重要。妊娠相关性血浆蛋白 A（PAPP－A）是一种胰岛素样生长因子（IGF）结合蛋白（IGFBP）－4 的蛋白酶，是不稳定性心绞痛的早期诊断指标。为此，我们建立了一种测定 PAPP－A 的超敏感酶联免疫吸附方法（ELISA），并检测了一些生化指标证实为急性冠状

动脉综合征患者的血清 PAPP－A。

该法的建立基于对一组抗体进行配对分析评价，确定 PAPP－A 检测的特异性及敏感性，并与传统检测方法之间进行相对比较。根据血清肌酸激酶（CK）MB 或肌钙蛋白 T（TnT）的水平，对血清标本进行分类，以此评估 PAPP－A 与心肌损伤的关系。结果显示，CK－MB 或 TnT 升高组的血清 PAPP－A 明显高于 CK－MB 正常组（$P<0.001$），且在样品 TnT 阳性组中 PAPP－A 与 TnT 之间存在强相关性（$r=0.59$，$P<0.001$）。对一组患者不同时间采集的系列样品进行检测，发现血清中 PAPP－A 与 TnT 表达量随时间的变化既有平行又可出现偏差。

所得数据与以下结论相吻合，即生化检测证实为急性冠脉综合征的患者血清 PAPP－A 表达升高。这充分表明，PAPP－A 与其他心脏标志物相关性的确定可受其相对释放动力学（出现时间与维持时间）的影响。有效的 PAPP－A 超敏感 ELISA 法将促进对这种疾病或其他与 IGF－PAPP－A 系统表达变化相关的病理生理条件进行系统研究。

3. 脑内淀粉样 β 蛋白沉积与 Alzheimer 病

Alzheimer 病的基本病理表现为以脑特定区域（如皮层和海马）的细胞缺失为特征的退行性变化过程。在显微镜下，淀粉样斑块被含有杂乱神经纤维团（微管相关蛋白因过度磷酸化而形成的成对螺旋状细丝，tau）的神经细胞所围绕，淀粉样的沉积常发生在小血管处。

有关 Alzheimer 病的病因正在进行深入细致的研究，最近已经取得了明显的进展，主要集中在淀粉样 β 多肽链（Aβ）的存在，它是 Alzheimer 病中所发现斑块的主要组成部分。淀粉样蛋白级联假说认为，Aβ 沉积是引起 Alzheimer 病人脑病理改变及其他变化（例如：继发性神经纤维缠结和血管改变）的原因。Aβ 源于一种较大的淀粉样前体蛋白（APP），其基因位于第 21 号染

色体靠近引起 Down 综合症（21 三体）的区域。Down 综合症病人在 50 岁左右时常患 Alzheimer 病。

APP 是一种跨膜蛋白，存在不同的异构体。Aβ 多肽链的长度可以从 39 到 42 个氨基酸不等，大多数淀粉样蛋白原属于后者。Aβ 从前体蛋白裂解释放后，可形成不溶的细胞外沉积物。APP 至少可以由三种酶分解，α－分泌酶产生一种可溶片段（sAPPα），它只包含 Aβ 部分。β 和 γ 分泌酶的作用是将 Aβ 从 APP 中分离出来。这些酶是如何被调节的仍需确定。有证据表明，神经元暴露于 Aβ 可以增加细胞内 Ca^{2+} 浓度。包括参与 tau 磷酸化的一些蛋白激酶，均受 Ca^{2+} 浓度的调节。因而，在杂乱的神经纤维团中会出现 tau 的增多和成对螺旋状细丝的形成。

某些 Alzheimer 病人已知有家族史，编码 APP 的第 21 号染色体基因突变的发现令人振奋，因其似乎与大多数 Alzheimer 病例有关。然而，这个遗传基因所涉及的只是少数病例。另外两种与一些家族性病例有关的基因已经被分离出来。它们编译的跨膜蛋白，与 Caenorhabditis elegans（一种蛔虫，已测得其基因组序列与人类基因组计划相关）的 SPE－4 蛋白质具有同源性。这种蛋白质参与了可溶性及膜结合性蛋白的转运。因此推测，新发现的基因编码的蛋白质（适当的名字为“presenilins”）可能参于 APP 的转运或加工过程。

目前，Alzheimer 病的最后确诊只能是在尸检时发现特征性斑块，治疗也没有特效药物。Alzheimer 病人脑部某些区域显示有脑源性神经生长因子缺陷，有关的可能治疗正在进行动物实验。

总之，在 Alzheimer 病中淀粉样蛋白起了重要作用，尽管仍不清楚在大多数病例中其沉积是原发的，还是继发于其他各种生化现象。最近与淀粉沉积无关的基因突变的发现打开了研究新思路，有可能会使我们对这种悲惨疾病的发生机制有更全面的了解。

（王江雁）

Unit Six

Text

Molecular Biology

What is molecular biology? The term has more than one definition. Some define it very broadly as the attempt to understand biological phenomena in molecular terms. But this definition makes molecular biology difficult to distinguish from another well known discipline, biochemistry. Another definition is more restrictive and therefore more useful: the study of gene structure and function at the molecular level. Molecular biology grew out of the disciplines of genetics and biochemistry. This hybrid discipline began with the earliest genetic experiments performed by Gregor Mendel in the mid – 19th century. By definition, the early work on genes cannot be considered molecular biology, or even molecular genetics, because early geneticists did not know the molecular nature of genes. Instead, we call it transmission genetics because it deals with the transmission of traits from parental organisms to their offspring. In fact, the chemical composition of genes was not known until 1944. At that point, it became possible to study genes as molecules, and the discipline of molecular biology was born.

Genes of all true organisms are made of DNA; certain viruses have genes made of RNA. DNA and RNA are chain – like molecules composed of subunits called nucleotides. DNA has a double – helical structure with sugar – phosphate backbones on the outside and base pairs on the inside. The three main activities of genes are information

storing, replication, and accumulating mutations. Proteins, or polypeptides, are polymers of amino acids linked through peptide bonds. Most genes contain the information for making one polypeptide and are expressed in a two – step process: transcription or synthesis of a mRNA copy of the gene, followed by translation of this message to protein. Prokaryotic gene expression can be summarized very briefly as follows: First, RNA polymerase transcribes a gene, or a set of genes, in an operon. Then, even while transcription is still occurring, ribosomes bind to the mRNA and translate it to make protein. However, the situation in eukaryotes is much more intricate. In eukaryotes, the compartments in which transcription and translation occur are different. Transcription takes place in the nucleus, whereas translation takes place in the cytoplasm. This means that transcription and translation cannot occur simultaneously as they do in prokaryotes. Instead, transcription has to finish, then the transcript has to make its way into the cytoplasm before translation can begin. This allows an interval between transcription and translation known as the posttranscriptional phase. Besides splicing, eukaryotic cells perform several other posttranscriptional modifications of their RNAs. Messenger RNAs are subject to two kinds of posttranscriptional modification, or processing, knoen as capping and polyadenylation. In capping, a special blocking nucleotide (a cap) is added to the 5' – end of a pre – mRNA. In polyadenylation, a string of AMPs (poly [A]) is added to the 3' – end of the pre – mRNA. These steps are essential for the proper function of mRNAs.

Although it is a very young discipline, it has an exceptionally rich history, and molecular biologists are now adding new knowledge at an explosive rate. Indeed, the pace of discovery in molecular biology, and the power of its techniques, has led many commentators

to call it a revolution. Because some of the most important changes in medicine over the next few decades are likely to depend on the manipulation of genes by molecular biologists, this revolution will touch everyone's life in one way or another. Thus, we are embarking on a study of a subject that is not only fascinating and elegant, but one that has practical importance as well. Can anyone be considered educated today who does not understand a little about molecular biology?

New Words

hybrid ['haibrid] n. 杂种,混血儿,混合物 adj. 混合的,杂种的
offspring ['ɔfspriŋ] n. （单复数同形）儿女，子孙，后代，产物
nucleotide ['nju:kliətaid] n. 核苷
replication [ˌrepli'keiʃən] n. 复制
polypeptide [ˌpɔli'peptaid] n. 多肽
polymer ['pɔlimə] n. 聚合体
transcription [træns'kripʃən] n. 转录
operon ['ɔpəˌrɔn] n. 操纵子
ribosome ['raibəsəum] n. 核糖体
eukaryote [ju'kæriəut] n. 真核细胞
polyadenylation ['pɔliə'denileiʃən] n. 多（聚）腺苷酸化
commentator ['kɔmenteitə] n. 评论员，讲解员
manipulation [məˌnipju'leiʃən] n. 处理，操作，操纵

Phrases and Expressions

molecular genetics 分子遗传学
parental organism 亲代
double - helical structure 双螺旋结构

base pairs　碱基对
amino acid　氨基酸
peptide bond　肽键
prokaryotic gene　原核基因
RNA polymerase　RNA 聚合酶
posttranscriptional phase　转录后阶段，转录后期

Questions

1. How to distinguish the discipline of molecular biology and biochemistry?
2. Please describe the structure of DNA.
3. What are the progress of transcription and translation?
4. Do you know how to separate the proteins or nucleic acids (DNA or RNA) from each other in the tissue? How to determine the quantities of the purified proteins, or DNA and RNA?
5. Make a speech or write a summary about the text.

Dialogue

To Purify DNA

Tom : Hi, Dennis. I want to know how to purify DNA. You know, it is very important for a molecular biology learner. But I am really a green - hand in it, and always confused in doing it. Could you help me?

Dennis : Ok, let's do it together. Please be confident, you can do it well. At first, please begin with the whole tissue. As soon as possible after excision, quickly mince tissue and freeze in liquid nitrogen.

Tom : Then, starting with grinding tissue between 200mg and 1g with a prechilled mortar and pestle, or crush with a hammer to a fine powder.

Dennis : Yeah. Then suspend the powdered tissue in 1.2ml digestion buffer per 100mg tissue. Well, Tom, pay more attention to the powder!

Tom : What's wrong with it?

Dennis : Clumps! There should be no clumps!

Tom : Ok, I will be more careful!

Dennis : Incubate the samples with shaking at 50℃ for 12 to 18 hours in tightly capped tubes. The samples will be viscous. After incubation, the tissue should be almost indiscernible. A sludge should be apparent from the organ samples. Thoroughly extract the samples with an equal volume of phenol / chloroform / isoamyl / alcohol. Phenol is extremely caustic, it is very dangerous! You should be cautious!

Tom : OK, what should we do next, I often at loss in the following step.

Dennis : Well, Tom, you are really hot – headed! OK, let's go on. Centrifuge 10 min at 1700g in a swinging bucket rotor. If the phases do not resolve well, add another volume of digestion buffer, omitting proteinase K, and repeat the centrifugation. If there is a thick layer of white material at the interface between the phases, repeat the organic extraction.

Tom : My God! Dennis, you are so great! You can remember everything so clearly!

Dennis : If you practice it more, you can do it better than me. Attention please! We will enter into the important part

of this trial. Transfer the aqueous (top) layer to a new tube and add 1/2 vol of 7.5 M ammonium acetate and 2 vol of 100% ethanol. The DNA should immediately form a stringy precipitate. Recover DNA by centrifugation at 1700g for 2 min.

Tom : Then, rinse the pellet with 70% ethanol. Decant ethanol and air dry the pellet. It is important to rinse well to remove residual salt and phenol.

Dennis : Right! At last, resuspend DNA at 1mg/ml in TE buffer until dissolved. Shake gently at room temperature or at 65℃ for several hours to facilitate solubilization. This is the whole process.

Tom : Thanks very much, Dennis! I will try it more, I believe I will do it well as you and give a big hand to the new learner.

Dennis : You are welcome! It's my honor to help you! Come on, you can do it better. Good luck to you!

Reading Material

1. The Chemical Structure of DNA of RNA

DNA and RNA have great chemical similarities. In their primary structures both are linear polymers composed of monomers, called nucleotides. Cellular RNAs range in length from less than one hundred to many thousands of nucleotides. Cellular DNA molecules can be as long as several hundred million nucleotides. These large DNA units in association with proteins can be stained with dyes and visualized in the light microscope as chromosomes.

In 1953, James D. Watson and Francis H. C. Crick proposed

correctly the double – helical structure of DNA, based on the analysis of x – ray diffraction patterns coupled with careful model building. Deoxyribonucleic acid (DNA), the genetic material, carries information to specify the amino acid sequences of proteins. It is transcribed into several types of ribosomal RNA (rRNA), which function in protein synthesis. Both DNA and RNA are long, unbranched polymers of nucleotides. Each nucleotide consists of a heterocyclic base linked via a five – carbon sugar (deoxyribose or ribose) to a phosphate group. DNA and RNA each contain four different bases. The purines adenine (A) and guanine (G) and the pyrimidine cytosine (C) are present in both DNA and RNA. The pyrimidine thymine (T) present in DNA is replaced by the pyrimidine uracil (U) in RNA. The bases in nucleic acids can interact via hydrogen bonds. The standard Watson – Crick base pairs are G – C, A – T (in DNA), and A – U (in RNA). Base pairing stabilizes the native three – dimensional structures of DNA and RNA. Adjacent nucleotides in a polynucleotide are linked by phosphodiester bonds. The entire strand has a chemical directionality: the 5' end with a free hydroxyl or phosphate group on the 5' carbon of the sugar, and the 3' end with a free hydroxyl group on the 3' carbon of sugar. Polynucleotide sequences are always written in the 5' – 3' direction (left to right). Natural DNA contains two complementary polynucleotide strands wound together into a regular right – handed double helix with the bases on the inside and the two sugar – phosphate backbones on the outside. Base pairing (A – T and C – G) and hydrophobic interactions between adjacent bases in the same strand stabilize this native structure.

Binding of protein to DNA can deform its helical structure, causing local bending or unwinding of the DNA molecule. Heat causes the

DNA strands to separate (denature) . The melting temperature of DNA increases with the percentage of G – C base pairs. Under suitable *conditions*, separated *complementary nucleic* acid strands will renature. Local unwinding of the DNA helix induces stress, which is relieved by twisting of the molecule on itself, forming supercoils. This process is regulated by topoisomerases, which can add or remove supercoils.

2. The Common Techniques Used in the Study of Molecular Biology

The most popular techniques that molecular biologists use to investigate the structure and function of genes start with cloned genes. Many use molecular separations. Many also use labeled tracers, and many rely on nucleic acid hybridization.

Gene cloning has revolutionized the discipline. Imagine that you are a geneticist in the year 1972. You want to investigate the function of eukaryotic genes at the molecular level. In particular, you are curious about the molecular structure and function of the human growth hormone (hGH) gene. What is the base sequence of this gene? How does RNA polymerase interact with this gene? What changes occur in this gene to cause conditions like hypopituitary dwarfism? Gene cloning neatly solves these problems. By linking eukaryotic genes to small bacterial or phage DNAs and inserting these recombinant molecules into bacterial hosts, one can produce large quantities of these genes in pure form.

It is very often necessary in molecular biology research to separate proteins or nucleic acids from each other. For example, we may need to purify a particular enzyme from a crude cellular extract in or-

der to use it or to study its properties. Or we may want to purify a particular RNA or DNA molecule that has been produced or modified in an enzymatic reaction, or we may simply want to separate a series of RNAs or DNA fragments from each other. So, some of the most common techniques should be used in such molecular separations, including gel electrophoresis of both nucleic acids and proteins, ion exchange chromatograpgy, and gel filtration chromatography.

Until recently, "labeled" has been virtually synonymous with "radioactive" because radioactive tracers have been available for decades, and they are easy to detect. Radioactive tracers allow vanishingly small quantities of substances to be detected. This is important in molecular biology because the substances we are trying to detect in typical experiment are present in very tiny amounts. Let us assume, for example, that we are attempting to measure the appearance of an RNA product in a transcription reaction. We may have to detect RNA quantities of less than a pictogram (pg; only one trillionth of a gram, or 10^{-12}g). Direct measurement of such tiny quantities by ultraviolet light absorption or by staining with dyes is not possible because of the limited sensitivities of these methods. On the other hand, if the RNA is radioactive we can measure small amounts of it easily because of the great sensitivity of the equipment used to detect radiography. The favorite techniques molecular biologists used to detect radioactive tracers include autoradiography, phosphorimaging, and liquid scintillation counting. Some very sensitive nonradioactive labeled tracers are also now available. These produce light (chemiliminescence) or colored spots.

The phenomenon of hybridization – the ability of one single – stranded nucleic acid to form a double helix with another single strand of complementary base sequence – is one of the backbones of modern molecular biology. Labeled DNA or RNA probes can be hybridized to

DNAs of the same, or very similar, sequence on a Southern blot. Modern DNA typing uses Southern blots and a battery of DNA probes to detect variable sites in individual animals, including humans. As forensic tool, DNA typing can be used to test parentage, to identify criminals, or to remove innocent people from suspicion. A Northern blot is similar to a Southern blot, but it contains electrophoretically separated RNAs instead of DNAs. The RNAs on the blot can be detected by hybridizing them to a labeled probe. The intensities of the bands reveal the relative amounts of specific RNA in each and the positions of the bands indicate the lenghths of the respective RNAs. Labeled probes can be hybridized to whole chromosomes to locate genes or other specific DNA sequences. This type of procedure is called in situ hybridization; if the probe is fluorescently labeled, the technique is called fluorescence in situ hybrization (FISH).

参考译文

课　文

分子生物学

什么是分子生物学？其定义不止一种。有的将其广义为从分子角度了解生物现象的科学。但这种定义使得分子生物学与另一众所周知的学科生物化学很难区分开来。另一种定义较局限，因而更有使用价值：在分子水平研究基因结构和功能的科学。

分子生物学的发展源于遗传学和生物化学。这一综合学科最早始于十九世纪中叶 Gregor Mendel 的遗传学实验。从定义上看，早期研究基因的工作不能认为是分子生物学，甚至也不属于分子遗传学的范畴，因为早期的遗传学家还不知道基因的分子特征。而我们只能称之为传递遗传学，因为它主要研究的是遗传性状自

亲代向子代的传递。事实上，直到 1944 年，人们才清楚基因的化学组成，才使将基因作为分子进行研究成为可能，从而诞生了分子生物学。

所有真正的有机生物体的基因由 DNA 组成，一些病毒的基因是 RNA。DNA 和 RNA 是由核苷酸亚单位组成的链状分子。DNA 是由外侧糖－磷酸骨架和内侧碱基对组成的双螺旋结构。基因的三个主要功能是：储存遗传信息、复制及累积突变。蛋白或多肽是通过肽键连接的氨基酸多聚体。大多数基因包含产生一种多肽的遗传物质，并经两个步骤进行表达：转录或基因 mRNA 的合成，并将此遗传信息翻译合成蛋白质。原核生物的基因表达可简单归纳为：首先，RNA 多聚酶在一种操纵子作用下转录一种或一套基因。然后，即使在转录正在进行时，核糖体也可与 mRNA 连接，并将其翻译合成蛋白质。但是，在真核生物中，这一过程就变得较为复杂了。在真核生物中，转录和翻译发生的部位是完全不同的。转录在胞核中进行，而翻译在胞浆中进行，这就意味着转录和翻译不能象在原核生物中那样同时进行。转录完成后，转录产物要设法在翻译前进入胞浆。这就在转录和翻译过程之间形成了一个被称为转录后期的间歇。除了剪接，真核细胞 RNA 还有其他几种转录后修饰。mRNA 可有两种转录后修饰，分别称为加帽和加 poly[A]尾。加帽时，一种特异性阻断性核苷酸(帽)加至 pre－RNA 的 5'端。加 poly[A]尾时，一连串 AMP(poly[A])被加至其 3'端。这些步骤对于保持 mRNA 的正常功能是十分必需的。

分子生物学虽然是一门新兴学科，但却具有异常丰富的历史，同时，分子生物学家现正以迅猛之势为其增添新知识。确实，分子生物学发展的步伐及其技术的威力使许多评论家称之为一场革命。因为，在不久的将来，医学的大多数重大改革可能均有赖于分子生物学家对基因的掌控，其变革将以这样或那样的方式触及每个人的生活。因此，我们正在从事一项既引人入胜又壮美的学科研究，同时又具有实践重要性。现今一点儿都不了解分

子生物学的人能称得上是受过医学教育吗?

对　话

分离 DNA

Tom：嗨！Dennis，我想知道怎样提取 DNA。你知道这个实验对于一个学习分子生物学的人来说很重要。但是我在这方面真的是初学者，而且总是不知所措。你能帮助我吗?

Dennis：没问题，我们一起做吧！要有信心，你就能做好。首先，我们从整个组织开始。尽量在组织切除后马上取材，迅速切碎组织并在液氮中冷冻保存。

Tom：随后，取 200mg 至 1g 大小的组织，在预冷的研钵中研碎或锤压成粉末状。

Dennis：是的，然后每 100mg 组织加入 1.2ml 裂解液混匀。Tom，注意组织碎块！

Tom：有什么问题吗?

Dennis：团块！一定不要有团块！

Tom：好的，我小心点儿。

Dennis：在密闭管中孵育标本，50℃轻摇 12 至 18 小时。标本会很粘。再加入等体积的苯酚/氯仿/异戊醇/酒精，以完全提取标本。经过孵育的组织几乎面目全非，裂解后的组织与器官组织标本有明显的区别。苯酚有很强的腐蚀性，很危险，一定要小心！

Tom：好，下一步怎么做？接下来的步骤我总是不清楚。

Dennis：Tom，你真是急脾气。好吧，让我们继续。以每分钟 1700g 的转速离心 10 分钟。如果分离不彻底，可以再加相同量不含蛋白酶 K 的裂解液，再次离心。如果在分离相表面有一厚层白色物质，就得重复上述组织提取过程。

Tom：天啊！Dennis，你太厉害了！你可以把每一步都记得这么

清楚。

Dennis：如果多练习，你可以做得比我更好。注意，我们要进入这个实验最关键的步骤了。把上层水相移入新试管，加入 1/2 量 7.5M 乙酸胺和 2 倍量的 100% 乙醇。DNA 应立刻形成粘性沉淀物，再以 1700g 的转速离心 2 分钟，分离出 DNA。

Tom：然后，用 70% 乙醇漂洗 DNA 沉淀。轻轻倒除乙醇，自然晾干沉淀。仔细漂洗去除残留的盐和苯酚很重要。

Dennis：没错！最后，在 1mg/ml TE 缓冲液中重悬 DNA 直至溶解。在室温下轻摇或置于 65℃ 数小时加速溶解。这就是 DNA 溶解的全部过程。

Tom：非常感谢你，Dennis！我会多多练习，相信我会做得与你一样好，并且也去帮助其他新学的人。

Dennis：你太客气了，帮助你很荣幸。你可以做得更好，祝你好运！

阅读材料

1. DNA 和 RNA 的化学结构

DNA 和 RNA 的化学成分极为相似。两者的基本结构都是由单体组成的线形多聚体，称为核苷酸。RNA 的长度由几十到数千个核苷酸组成不等，而细胞 DNA 分子则可由数十亿个核苷酸构成。这些与蛋白相关的较大的 DNA 单位可被染料染色，并以染色体的形式在光学显微镜下被观察到。

1953 年，James D. Watson 和 Francis H. C. Crick 根据对所建立模型的 X 射线衍射图谱分析，提出了准确的 DNA 双螺旋结构理论。脱氧核糖核酸（DNA）作为遗传物质，携带着蛋白质中可排列氨基酸顺序的信息。DNA 将遗传信息转录给各种核糖核酸（RNA），包括信使 RNA（mRNA）、转移 RNA（tRNA）和核糖体 RNA（rRNA），它们均在蛋白质合成中发挥作用。DNA 和

RNA 都是很长的无支链核苷酸多聚体。每个碱基通过一个戊糖（去氧核糖或核糖）和一个磷酸基团相连构成核苷酸。DNA 和 RNA 都包含 4 个不同的碱基，腺嘌呤（A）、鸟嘌呤（G）、胞嘧啶（C）都存在于 DNA 和 RNA 中。DNA 里的胸腺嘧啶（T）在 RNA 里则由尿嘧啶（U）代替，核酸中的碱基通过氢键相互连接在一起。标准的沃森－克里克碱基配对为 G－C、A－T（DNA 中）和 A－U（RNA 中）。DNA 和 RNA 通过碱基配对稳固了其自身的三维结构。相邻的单核苷酸通过磷酸二酯键相连构成多核苷酸。整个多核苷酸序列是有化学方向性的：与戊糖基相连的 5'位碳原子连接一个游离羟基或磷酸基团，与戊糖基相连的 3'位碳原子连接一个游离羟基。通常多核苷酸序列的书写方向（由左向右）是 5'→3'方向。天然 DNA 包含两个缠绕在一起形成规则右旋双螺旋结构的互补多核苷酸链，其中碱基在内侧，两条糖－磷酸骨架位于外侧。碱基相互配对（A－T 和 G－C）和同一链上相邻碱基间的疏水性相互作用对其天然结构起到稳固作用。

蛋白质与 DNA 结合会造成 DNA 螺旋结构变形，引起 DNA 分子的弯曲或伸直。加热可引起 DNA 链的解离（变性），DNA 的解链温度随着 G－C 配对碱基百分含量而增加。在合适的条件下，分离的互补核酸链会复性。DNA 螺旋的局部解旋会导致应力，分子本身会弯曲以减轻应力，形成超螺旋结构，这个过程由拓扑异构酶调节以增加或解除超螺旋。

2. 分子生物学研究中常用的实验技术

分子生物学家研究基因结构和功能的常用技术，首先是基因克隆，另外还有分子分离、标记示踪和核酸杂交技术。

基因克隆技术给这一学科带来了革命。设想你是 1972 年时期的遗传学家，想在分子水平研究原核生物基因的功能，特别是对人生长激素（hGH）基因的分子结构和功能十分感兴趣。那么，这种基因的基本序列是什么？RNA 聚合酶如何与基因发生

相互作用？其基因发生怎样的改变时导致形成诸如垂体功能减退性侏儒症之类的表现？应用基因克隆技术就可以很好地解决这些问题。通过将真核生物基因连接至细菌或噬菌体 DNA，再将这种重组分子插入至细菌宿主，就可产生这种基因的大批量纯产品。

在分子生物学研究中，经常需要将蛋白质或核酸彼此分离出来。例如，我们需要从细胞的粗提取物中分离出某种特殊的酶，以使用或研究其特性。或者，我们想要分离出可在酶促反应中产生或被修饰的一种特殊 RNA 或 DNA 分子。或者，我们只是想分离出一系列 RNA 或 DNA 片段。因此，在进行这种分子分离时，需要采用一些最普通的技术，包括核酸和蛋白质的凝胶电泳技术、离子交换色谱法和凝胶过滤色谱法。

直至目前，“标记”实际上仍是“放射性”的同义词，因为放射示踪这种易于检测的技术已被应用了几十年，它可将正在逐渐消失的微量物质检测出来。这一点在分子生物学中十分重要，因为在典型的分子生物学实验中，我们试图检测的物质极微量。让我们设想一下，比如我们正试图在转录反应中检测一种 RNA 产物的存在，检测 RNA 量低于 1pg（pg，仅为 1g 的兆分之一，即 10^{-12}g）。采用紫外线吸收或染料染色技术不可能直接检测到如此微量的物质，因为这些方法的敏感性有限。但是，如果 RNA 具有放射性，我们就可以轻易检测到这些微量物质，因为放射性检测设备的敏感性很强。分子生物学家最喜欢的放射性示踪检测技术包括放射自显影技术、磷酸成像和液闪计数。其他一些非常敏感的非放射性标记示踪技术现在同样可用，它们可产生光斑（化学发光）或色斑。

杂交，即一条单链核酸与另一条单链互补碱基序列形成一条双螺旋结构，是现代分子生物学的基础之一。标记的 DNA 或 RNA 探针可采用 Southern 印迹与相同或相似序列的 DNA 杂交。现代 DNA 分型采用 Southern 印迹和一组 DNA 探针检测动物（包括人类）的不同位点。作为一种法医检测手段，DNA 分型可用

于亲子鉴定、确认罪犯或解除犯罪嫌疑。Northern 印迹类似于 Southern 印迹，但这项技术电泳分离的是 RNA 而不是 DNA。印迹中的 RNA 可通过与标记探针杂交而进行检测。杂交条带强度可反映特异性 RNA 的含量，条带位置显示各 RNA 的长度。标记探针可与整条染色体杂交，以定位基因或其他特异性 DNA 序列，这一过程称为原位杂交。若探针是荧光标记的，则称为荧光原位杂交（FISH）。

（朱　辉　刘欣燕）

Unit Seven

Text

Medical Genetics

Medical genetics is a relatively new field of study. The chromosomal basis of many recognizable syndromes, for instance, was not known until 1958 when the cause of Down syndrome (trisomy 21) was discovered. In the 1970's and 80's, it was possible to catalog what was known about single gene disorders in a single text. However, through innovative research in a number of different fields, knowledge about genes and genetic disorders is expanding at such a rate that catalogs of genetic disorders are now out of date at the time of printing. The integration of basic research and clinical application has spawned a new specialty in medicine, Medical Genetics, which was officially recognized as a medical subspecialty by the American Board of Medical Subspecialty in 1993.

Genetics is essential in many areas of medicine. It is now possible

to identify the presence of deleterious genes and chromosomal abnormalities prior to implantation or birth. The underlying causes of many syndromes and genetic disorders have been identified and improved treatment strategies are being developed. Genetic tests can also be used to establish a diagnosis or identify gene carriers prior to the onset of symptoms. Additionally, DNA based molecular diagnosis is replacing or complementing routine laboratory tests.

The role that genetics plays in the etiology of common diseases has captured the attention of the general public. It is not uncommon to peruse a popular magazine and find articles on prenatal diagnosis, the genetics of breast cancer or the latest in gene therapy. As our knowledge of medical genetics expands and public interest in the subject grows, the challenge for health care providers is to recognize individuals who might benefit from a genetics referral, to share accurate information about the new screening tests that are being developed for common and chronic diseases, and to respond to the unique problems in the care of patients and families with genetic afflictions.

New Words

genetics [dʒi'netiks] n. 遗传学
chromosome ['krəuməsəum] n. 染色体
syndrome ['sindrəum] n. 综合征
trisomy ['traisəumi] n. 三体,三(染色)体性,三(染色)体细胞
innovative ['inəuveitiv] adj. 创新的，革新（主义）的
integration [ˌinti'greiʃən] n. 综合
deleterious [ˌdeli'tiəriəs] adj. 有害的，有毒的
symptom ['simptəm] n. 症状，征兆
etiology [ˌi:ti'ɔlədʒi] n. 病因学，病原论
peruse [pə'ru:z] v. 细读

prenatal [ˈpriːˈneitl] adj. 出生以前的
chronic [ˈkrɔnik] adj. 慢性的，延续很长的
affliction [əˈflikʃən] n. 痛苦，苦难；痛苦之因，痛苦之事

Phrases and Expressions

Down syndrome　唐氏综合征
single gene disorder　单基因病
genetic disorder　遗传病
out of date　不合时宜，过时
American Board of Medical Subspecialty　美国医学分类委员会
common disease　常见病
breast cancer　乳腺癌
health care　卫生保健

Questions

1. Do you know the genetics detail of Down syndrome?
2. Do you know the latest catalog of genetic disorders?
3. What should the health care providers be challenged as the knowledge of medical genetics expanded and the public interest in this subject grew?
4. Please describe the latest gene therapy of breast cancer as possible as you can.
5. What are the purposes of genetic test undergoing presently?
6. Make a speech or write a summary about the text.

Dialogue

About Genetic Disorder

Teacher: Good morning, students. Today, we will have a quiz about

the basic knowledge of Genetics. Please answer my questions actively. Ok, now who can tell me the difference between gene and genome?

Alice : Gene is the segment of DNA that contains all the information needed for regulated synthesis of RNA or protein product. Genome is the entire DNA sequence content of an organism.

Teacher : *Good job. How many classifications of genetic disorders?*

Bob : Single – gene disorders, chromosome disorders and multifactorial disorders.

Teacher : Can you tell me their distinguishing characteristics?

Bob : Single – gene disorders are caused by mutations in individual genes. Mutations may be present in only one or both copies of a gene, usually exhibit obvious and characteristic pedigree patterns. Chromosome disorders due to an excess or deficiency of the genes contained in whole chromosomes or chromosome segments, for example, Trisomy 21 – Down syndrome, Trisomy 18 – Edward syndrome, XXY – Klinefelter syndrome, XO – Turner syndrome, 22q11 micro – deletion, and etc. It can affect about 7 per 1000 infants, account for about half of all spontaneous first – trimester abortions. Multi – factorial disorders result from both environmental and genetic factors. Relative importance of genetic factors is variable. Familial tendency apparent but do not follow the characteristic pedigree patterns of single – gene disorders. For example, neural tube defects, asthma, diabetes, hypertension, coronary heart disease, cancer, and etc.

Teacher : Excellent.

Reading Material

1. Chromosomes

It is well known that DNA (deoxyribonucleic acid) is the blueprint of life. DNA provides the codes for the structural and enzymatic proteins that make up every cell. DNA is packaged into units called chromosomes. The chromosome number varies in different species. In humans there are 46 chromosomes, or 23 pairs of chromosomes (diploid), in every cell except the mature egg and sperm which have a set of 23 chromosomes (haploid). If the chromosomes in a single cell were stretched out and laid end to end, the DNA would be two meters long.

Chromosomes are visible only during cell division, when the DNA is supercoiled and condensed to facilitate distribution into daughter cells. Cell division in somatic cells (mitosis) results in the creation of daughter cells with the same number of chromosomes as the original cell, a total of 46 chromosomes. Cell division in the germ cells, eggs and sperm (meiosis), results in the creation of daughter cells with half the number of chromosomes as the original cell, a total of 23 chromosomes. This reduction in the number of chromosomes is important so that the original number of 46 chromosomes is restored following fertilization of the egg by the sperm.

The chromosome constitution of an individual (karyotype) can be analyzed following tissue culture of an appropriate sample. The most commonly used sample is blood (using the white blood cells or lymphocytes) since it is the most accessible. However, other samples are used depending upon the indication: amniotic fluid cells, to analyze the karyotype of the fetus; products of conception, to analyze the

cause of a miscarriage or stillbirth; bone marrow cells, to diagnose the presence or type of leukemia; and skin, to determine the presence of another cell line (mosaicism).

Since cells have to be grown in culture, it is important that samples are received in the laboratory within 24 to 48 hours after collection. The cells are grown in media for three days to two weeks depending on the sample source. Cell division is arrested during metaphase, when the chromosome material is condensed. Following hypotonic treatment and fixation, the cells are dropped on a slide and then stained. At least 20 metaphase spreads are analyzed and 2 or 3 metaphase spreads are photographed. The chromosomes are arranged to create a karyotype.

Chromosomes vary in size and in shape. The pairs of autosomal chromosomes are arranged in a karyotype from the biggest, #1, to the smallest, #22. The sex chromosomes are placed to the right of the smallest autosomal chromosomes. Chromosomes vary in shape depending upon the position of the centromere, the structure that holds the two arms of the chromosomes together. If the centromere is in the middle, the chromosome is metacentric and the chromosome arms are equal in size. If the centromere is off center, the chromosome is submetacentric with a short arm labeled p (for petite) and a long arm labeled q (the next letter after p). If the centromere is close to the end, the chromosome is acrocentric and the very short arm consists of a stalk and a knob (satellite). Based upon size and shape, chromosomes are divided into eight groups: A (1 to 3), B (4 and 5), C (6 to 12), D (13 to 15), E (16 to 18), F (19 and 20), G (21 and 22) and the sex chromosomes, XX in females and XY in males.

2. Multifactorial Inheritance

The most common cause of genetic disorders is multi – factorial or polygenic inheritance. Traits that are due to the combined effects of multiple genes are polygenic (many genes) . When environmental factors also play a role in the development of a trait, the term multi – factorial is used to refer to the additive effects of many genetic and environmental factors. Expression of these traits may follow a normal, or " bell – shaped," curve. Examples of multi – factorial traits include cleft lip and palate, congenital hip dislocation, schizophrenia, diabetes and neural tube defects such as spine bifida.

Multi – factorial conditions tend to run in families, but the pattern of inheritance is not as predictable as with single gene disorders. The chance of recurrence is also less than the risk for single gene disorders. The degree of risk of a multi – factorial disorder occurring in relatives is related to the number of genes they share in common with the affected individual. The closer the degree of relationship is, the more genes are in common. The degree of risk also increases with the degree of severity of the disorder.

Although multi – factorial conditions run in families, the risk is generally less than the 25% or 50% seen in Mendelian conditions. Identical twins that are exactly alike genetically, do not always have the same condition when inheritance is multi – factorial. This indicates that there are nongenetic factors that also play a role in the expression of multi – factorial traits. For instance, the risk of coronary heart disease increases with smoking or obesity. The risk of emphysema in individuals with alpha – 1 – antitrypsin deficiency increases greatly with smoking. Maternal alcohol abuse or uncontrolled diabetes increases the risk of having a child with a congenital heart defect.

Empiric risks are used to predict the recurrence of a multi – factorial disorder. This is a risk that is based on epidemiologic and population studies and on mathematical models.

For many multi – factorial or polygenic disorders, parents who have had one affected child have a 3 ~ 5% risk in future pregnancies of having another affected child. Affected individuals have a similar risk in future progeny. More distant relatives, however, have a lower recurrence risk.

In conditions inherited in a multi – factorial fashion, the risk may depend on the sex of the affected individual. For example, pyloric stenosis is a multi – factorial disorder that occurs five times more frequently in males than in females. If a female child has pyloric stenosis, her risk and her parent's risk of having another affected child would be higher than if a male child has pyloric stenosis. Occurrence in a female suggests a greater genetic liability; presumably more abnormal genes are segregating in the family.

3. Gene Involved in Prion Disease Identified

Recently, UK investigators reported the identification of three genetics linkage sites that may be involved in susceptibility to prion disease. The investigators, led by John Collinge from the Prion Unit at the Imperial College School of Medicine, London, identified mouse prion susceptibility alleles, which may be relevant to understanding human infection with variant Creutzfeld – Jakob disease (vCJD).

The investigators crossed two different inbred lines of mice that had the same prion genotype but markedly different incubation periods when challenged with prions. Incubation times were measured in 1009 animals inoculated with scrapie prions.

After DNA extraction, genome screening revealed three regions of highly significant linkage on chromosomes 2, 11 and 12. Three are likely to be corresponding genes in human beings that have the same role, the investigators propose, because of the sequence conservation between the mouse and human genome. Discovery of such loci in human beings may allow at – risk individuals to be identified.

This is the first step in our understanding of genetic susceptibility to prions, Collinge told The Lancet: "It will be very important to identify and characterize these new genes to help us understand the risks involved." Such work may also help early diagnosis and risk management to limit spread of these diseases and also to cast light on the fundamental processes of prion disease.

In the human prion protein gene a polymorphism occurs at codon 129 where either a methionine (M) or valine (V) may be encoded. All the cases of vCJD identified so far are from the MM genotype. "It is likely that within the MM group there are differing degrees of susceptibility to prion disease and that the human counterparts of the genes we are now locating in mice will be crucial to this." says Collinge, "Those patients we have seen so far with vCJD may be those genetically disposed to have the shortest incubation periods."

参考译文

课　文

医学遗传学

医学遗传学是一门相对较新的研究领域。例如，直到 1958 年唐氏综合征（21 三体）的病因被发现后，许多已知综合征的染色体发病基础才得以确认。在二十世纪 70 年代和 80 年代，仅

在一本有关单基因遗传病的书中才将已知的单基因病进行了分类；但许多不同领域的研究不断更新，有关基因和遗传病的知识迅速增多，以至于这本书在印刷时对遗传病的分类现在已经过时。基础研究和临床应用的结合，使医学领域产生了一门新学科，即医学遗传学，并在 1993 年由美国医学分类委员会正式认定为一门医学分科。

遗传学在许多医学领域都是必需的。现在已经可以在胚胎植入或出生前确定有害基因和染色体畸变的存在。许多综合征和遗传病的病因已被确定，治疗手段也得到了改进提高。在临床症状出现前，遗传学检查可用于确诊和筛查有害基因携带者。另外，DNA 分子诊断正在取代或辅助常规的实验室检查。

遗传学在常见病的病因学研究中所发挥的作用已引起普遍关注。仔细阅读一本流行杂志，不难发现关于产前诊断、乳腺癌的遗传学或最新基因治疗方面的文章。随着医学遗传学知识的增加以及大家对此学科兴趣的提高，卫生保健医务人员将面临以下挑战：确定遗传咨询服务对象，共享常见病和慢性病最新普查的准确信息，在护理过程中回答患者和受遗传影响家庭所面临的特殊难题。

对　话

有关遗传病

老师： 同学们，早上好。今天，我们将就有关遗传学的基本知识进行一次小测验，希望每一位都能积极回答问题。好，现在谁能告诉我基因和基因组的区别？

Alice： 基因是 DNA 的片断，它包含着调节 RNA 或蛋白质合成的全部遗传信息。而基因组是指一个生物体全部的 DNA 序列。

老师： 很好。那么，遗传病分几类？

Bob： 单基因病、染色体病和多基因病。

老师：你能说出这 3 种遗传病各有何特点吗？

Bob：单基因病是由单个基因突变而引起的，突变只发生在一个基因或一对基因之间，通常有明显的、特征性的家族表现。染色体病是由于整条染色体或部分染色体增加或缺失导致基因的改变，例如，21 三体唐氏综合征、18 三体爱德华综合征、XXY 克氏综合征、X0 杜氏综合征、22q11 部分缺失等。新生儿发生率为 7‰，相当于发生早期自然流产病例的一半。多基因病既有环境因素也受遗传因素的影响，遗传因素作用的相对重要性各有不同；有明显的家族倾向，但并不表现出单基因病的家族遗传特征，例如，神经管畸形、哮喘、糖尿病、高血压、冠心病、癌症等。

老师：非常棒。

阅读材料

1. 染色体

众所周知，DNA 是生命的蓝图。DNA 为构成每一个细胞的结构和酶蛋白提供遗传密码。DNA 包裹成被称为染色体的单位，不同物种的染色体数目不同。人类除了精、卵细胞只有一套 23 条染色体（单倍体）外，其他每个细胞均有 46 条或 23 对染色体（二倍体）。如果把单个细胞的全部染色体展开拉长并且头尾相连，DNA 将达 2 米长。

染色体只有在细胞分裂时才能观察到，这时 DNA 超螺旋且浓缩以便分配到子代细胞中。体细胞的细胞分裂（有丝分裂）导致新生子代细胞与亲代细胞有相同数量的总共 46 条染色体。精、卵细胞的分裂（减数分裂）导致新生子代细胞中只有亲代细胞的半数 23 条染色体。这种染色体数量的减少对于精卵结合后恢复到亲代 46 条染色体数目是非常重要的。

标本的组织培养可用于分析个体的染色体组成（核型）。最

常用的标本是血液（使用其中的白细胞或淋巴细胞），因为它最容易获得。但其他标本的使用根据不同的目的，羊水细胞用于分析胎儿核型，胚胎产物用于分析流产或死胎的原因，骨髓细胞用于诊断白血病及判断型别，皮肤用于确认是否有其他细胞系（嵌合组织）。

由于细胞只有经过培养才能生长，因此，在采集标本后 24 至 48 小时内将标本送到实验室非常重要。根据标本的来源，细胞在培养基中生长 3 天到两个星期不等。在分裂中期，当染色体浓缩时，细胞分裂中止，随后低渗处理并固定，将细胞滴到玻片上染色。至少要分析 20 个中期分裂相并拍摄 2 或 3 张照片后，将染色体排列以进行核型分析。

染色体的大小和形态各不相同。1～22 号常染色体由大到小成对排列在核型中，性染色体放在最小的常染色体右侧。染色体的形态差别是根据着丝粒的位置，着丝粒是将两个染色体臂连在一起的结构。如果着丝粒位于中央，该染色体是中央着丝粒染色体，染色体臂大小均等；如果着丝粒偏离中央，该染色体称为亚中央着丝粒染色体，且短臂用符号 p（petite）表示，长臂用符号 q（p 后面的字母）表示。如果着丝粒靠近末端，该染色体就是近端着丝粒染色体，一个非常短的臂且有一个随体。根据大小和形态，染色体被分成 8 个组：A 组（1～3 号），B 组（4～5 号），C 组（6～12 号），D 组（13～15 号），E 组（16～18 号），F 组（19～20 号），G 组（21～22 号）和性染色体，女性为 XX，男性为 XY。

2. 多因子遗传

遗传病的最常见病因是多因子或多基因遗传，其发病特点是多基因共同作用。在发病特点上环境因素也发挥作用，因此，“多因子”这一术语是指多基因和环境因素的共同影响。多基因病的遗传特点表现为正态分布钟形曲线。多因子病常见的有唇裂及腭裂、先天性髋关节脱位、精神分裂症、糖尿病和神经管缺陷

（如脊柱裂）。

多基因病有家族遗传倾向，但遗传方式与单基因病有本质不同，再发风险也远低于单基因病。多因子病亲属发病风险的高低与他们所携带的与患者一样的有害基因数量有关。亲缘关系愈近，有害基因越多，多基因病发病风险愈高，病情愈重。

尽管多因子遗传表现为家族倾向，但其发病风险却低于孟德尔遗传的 1/4 或 1/2。同卵双生子遗传上完全相同，但存在多基因遗传时，他们并不完全相同。这说明多因子病的表型还受非遗传因素影响。例如，冠心病的发病风险会随着吸烟和肥胖而增高；由于 α1 抗胰蛋白酶缺陷而引起的慢性阻塞性肺气肿的风险随吸烟而增加；孕妇酗酒和患有糖尿病，则胎儿患先天性心脏缺损的风险增加。

经验风险可用于预测多因子病的再发。这种风险预测建立在流行病学和人群研究以及数学模式的基础上。

就许多因子或多基因病来说，如果一对夫妇已生了一个患儿，则再次妊娠后的胎儿发病风险为 3% ~5%。患病个体妊娠时也有相似的风险。但是，亲缘关系愈远，再发风险愈低。

在多因子遗传中，发病风险有时也与患者的性别有关。例如，先天性幽门狭窄是一种多因子病，男性发病率比女性高 5 倍。与患病男孩相比，如果一个女孩患有先天性幽门狭窄，那么其子女的发病风险和其父母再生出一个患儿的风险要高。女性发病表明更高的遗传风险，可能会使这个家庭带有更多的有害基因。

3. 朊病毒感染性疾病相关基因被证实

最近，英国的研究人员宣布，他们已确定了三个与朊病毒所致疾病有关的基因位点。这些研究人员由 John Collinge 带领，来自伦敦的英国皇家医学院的朊病毒小组，他们证实了小鼠朊病毒易感等位基因的存在，这可能与研究人类变异型 Creufzfed – Jakob 病（vCJD）有关。

研究者将两种不同品系的小鼠进行杂交，这些小鼠的朊病毒感染相关基因型相同，但受朊病毒感染时，潜伏期明显不同。其潜伏期是通过对 1009 只动物接种瘙痒病朊病毒后而确定的。

提取 DNA 后，基因组扫描显示，在第 2、11、12 号染色体上，有三个高度连锁的基因区，有可能与人类相关基因一致，且具有相同的功能。研究人员认为，这是由于人和小鼠染色体基因序列有保守性。如能在人类发现类似的基因区，有助于鉴别高危人群。

这是了解朊病毒基因易感性的第一步。Collinge 在《柳叶刀》杂志中说："这将对证实这些新基因并确定其特征，以帮助我们了解感染的危险是十分关键的"。这项研究还有助于早期诊断和危险控制，以限制本病的传播，还可使人们关注朊病毒性疾病的基本发病过程。

人类朊病毒蛋白基因多态性发生在第 129 密码子上，该位点既可编码蛋氨酸（M），也可编码缬氨酸（V）。迄今为止，所有的 vCJD 病例都是通过 MM 基因型确定的。"这可能是在 MM 基因型人群中存在着对朊病毒不同的易感性，因此，目前在小鼠体内确定与人类相对应的基因方面的研究至关重要"。Collinge 说，"迄今所看到的 vCJD 病患者，可能就是那些在遗传上有最短潜伏期倾向的人"。

（崔　澂　齐丽荣）

Unit Eight

Text

Pathogenic Biology

Pathogenic biology, a very large discipline, in which includes

medical microbiology and parasitology. And many groups of branch about related pathogenic microbiology such as bacteriology, virology, mycology and etc contribute to the discipline of medical microbiology.

Introduction to Bacteriology

Bacteria are single – celled microorganisms that lack a nuclear membrane, are metabolically active and divide by binary fission. Medically they are a major cause of disease. The discipline of bacteriology evolved from the need of physicians to test and apply the germ theory of disease and from economic concerns relating to the spoilage of foods and wine.

Major advances in bacteriology over the last century resulted in the development of many effective vaccines (eg. pneumococcal polysaccharide vaccine, diphtheria toxoid, and tetanus toxoid) as well as of other vaccines (eg. cholera, typhoid, and plague vaccines) that are less effective or have side effects. Another major advance was the discovery of antibiotics. These antimicrobial substances have not eradicated bacterial diseases, but they are powerful therapeutic tools. Their efficacy is reduced by the emergence of antibiotic resistant bacteria (now an important medical management problem).

Most diseases now known to have a bacteriologic etiology have been recognized for hundreds of years. Some were described as contagious in the writings of the ancient Chinese, centuries prior to the first descriptions of bacteria by Anton van Leeuwenhoek in 1677. There remain a few diseases (such as chronic ulcerative colitis) that are thought by some investigators to be caused by bacteria but for which no pathogen has been identified. Occasionally, a previously unrecognized disease is associated with a new group of bacteria. An example is Legionnaire's disease, an acute respiratory infection caused by the previously unrecognized genus, Legionella. Also, a newly recognized

pathogen, Helicobacter, plays an important role in peptic disease. Another important example, in understanding the etiologies of venereal diseases, was the association of at least 50 percent of the cases of urethritis in male patients with Ureaplasma urealyticum or Chlamydia trachomatis.

Recombinant bacteria produced by genetic engineering are enormously useful in bacteriologic research and are being employed to manufacture scarce biomolecules (eg. interferons) needed for research and patient care. The antibiotic resistance genes, while a problem to the physician, paradoxically are indispensable markers in performing genetic engineering. Genetic probes and the polymerase chain reaction (PCR) are useful in the rapid identification of microbial pathogens in patient specimens. Genetic manipulation of pathogenic bacteria continues to be indispensable in defining virulence mechanisms. As more protective protein antigens are identified, cloned, and sequenced, recombinant bacterial vaccines will be constructed that should be much better than the ones presently available.

In developed countries, 90 percent of documented infections in hospitalized patients are caused by bacteria. These cases probably reflect only a small percentage of the actual number of bacterial infections occurring in the general population, and usually represent the most severe cases. In developing countries, a variety of bacterial infections often exert a devastating effect on the health of the inhabitants. Malnutrition, parasitic infections, and poor sanitation are a few of the factors contributing to the increased susceptibility of these individuals to bacterial pathogens. The World Health Organization has estimated that each year, 3 million people die of tuberculosis, 0.5 million die of pertussis, and 25,000 die of typhoid. Diarrheal diseases, many of which are bacterial, are the second leading cause of death in

the world (after cardiovascular diseases), killing 5 million people annually.

Many bacterial diseases can be viewed as a failure of the bacterium to adapt, since a well – adapted parasite ideally thrives in its host without causing significant damage. Relatively well – adapted nonvirulent microorganisms can cause disease under special conditions – for example, if they are present in unusually large numbers, if the host's defenses are impaired, (eg. AIDS and chemotherapy) or anaerobic conditions exist. Pathogenic bacteria constitute only a small proportion of bacterial species; many nonpathogenic bacteria are beneficial to humans (eg. intestinal flora produce vitamin K) and participate in essential processes such as nitrogen fixation, waste breakdown, food production, drug preparation, and environmental bioremediation. The medical microbiology emphasizes bacteria that have direct medical relevance.

Introduction to Virology

Epidemiologic studies show that viral infections in developed countries are the most common cause of acute disease that does not require hospitalization. In developing countries, viral diseases also exact a heavy toll in mortality and permanent disability, especially among infants and children. Emerging viral diseases such as those due to HIV, ebolavirus and hantavirus, appear regularly. Now that antibiotics effectively control most bacterial infections, viral infections pose a relatively greater and less controlled threat to human health. Some data suggest that the already broad gamut of established viral diseases soon may be expanded to include other serious human ailments such as juvenile diabetes, rheumatoid arthritis, various neurologic and immunologic disorders, and some tumors.

Viruses are small, subcellular agents that are unable to multiply

outside a host cell (intracellular, obligate parasitism). The assembled virus (virion) is formed to include only one type of nucleic acid (RNA or DNA) and, in the simplest viruses, a protective protein coat. The nucleic acid contains the genetic information necessary to program the synthetic machinery of the host cell for viral replication. The protein coat serves two main functions: first, it protects the nucleic acid from extracellular environmental insults such as nucleases; Secondly, it permits attachment of the virion to the membrane of the host cell, the negative charge of which would repel a naked nucleic acid. Once the viral genome has penetrated and thereby infected the host cell, virus replication mainly depends on host cell machinery for energy and synthetic requirements.

The various virion components are synthesized separately within the cell and then assembled to form progeny particles. This assembly type of replication is unique to viruses and distinguishes them from all other small, obligate, intracellular parasites. The basic structure of viruses may permit them to be simultaneously adaptable and selective. Many viral genomes are so adaptable that once they have penetrated the cell membrane under experimental conditions, viral replication can occur in almost any cell. On the other hand, intact viruses are so selective that most virions can infect only a limited range of cell types. This selectivity exists largely because penetration of the nucleic acid usually requires a specific reaction for the coat to attach to the host cell membrane and some specific intracellular components.

Viruses are distinct among microorganisms in their extreme dependence on the host cell. Since a virus must grow within a host cell, the virus must be viewed together with its host in any consideration of pathogenesis, epidemiology, host defenses, or therapy.

The intracellular location of the virus often protects the virus

against some of the host's immune mechanisms; at the same time, this location makes the virus vulnerable because of its dependence on the host cell's synthetic machinery, which may be altered by even subtle physical and chemical changes produced by the viral infection (inflammation, fever, circulatory alterations, and interferon).

Knowledge of the pathogenetic mechanisms by which virus enters, spreads within, and exits from the body also is critical for correct diagnosis and treatment of disease and for prevention of spread in the environment. Effective treatment with antibody – containing immunoglobulin requires knowing when virus is susceptible to antibody (for example, during viremic spread) and when virus reaches target organs where antibody is less effective. Many successful vaccines have been based on knowledge of pathogenesis and immune defenses. Comparable considerations govern treatment with interferon.

Introduction to Mycology

Fungi are eukaryotes. They possess a nucleus enclosed by a nuclear membrane, a rigid cell wall, endoplasmic reticulum, and mitochondria like those of plant and animal cells. These structures differ substantially from those of bacteria. Of the approximately 70, 000 recognized species of fungi, about 300 are known to cause human infections. Fungal diseases of healthy humans tend to be relatively benign, but the few life – threatening fungal diseases are extremely important. Fungal diseases are an increasing problem due to the use of antibacterial and immunosuppressive agents. Individuals with an altered bacterial flora or compromised defense mechanisms (eg. AIDS patients) are more likely than healthy people to develop opportunistic fungal infections such as candidiasis. Consequently, opportunistic fungal pathogens are increasingly important in medical microbiology.

Host defenses against fungi are similar to those utilized against bacterial diseases, except that the cell – mediated response is extremely important. Nonspecific immunity and cell – mediated immunity seem to be the most important means by which humans resist or eliminate fungal pathogens.

Introduction to Parasitology

Medical parasitology traditionally has included the study of three major groups of animals: parasitic protozoa, parasitic helminths (worms), and those arthropods that directly cause disease or act as vectors of various pathogens. Although parasitology had its origins in the zoologic sciences, it is today an interdisciplinary field, greatly influenced by microbiology, immunology, biochemistry, and other life sciences.

Infections of humans caused by parasites number in the billions and range from relatively innocuous to fatal. The diseases caused by these parasites constitute major human health problems throughout the world. (For example, approximately 30 percent of the world's population is infected with the nematode *Ascaris lumbricoides*.) The incidence of many parasitic diseases (eg. schistosomiasis, malaria) have increased rather than decreased in recent years. Other parasitic illnesses have increased in importance as a result of the AIDS epidemic (eg. cryptosporidiosis, *Pneumocystis carinii* pneumonia, and strongyloidiasis).

The unicellular parasites (protozoa) and multicellular parasites (helminths, arthropods) are antigenically and biochemically complex, as are their life histories and the pathogenesis of the diseases they cause. During their life, parasitic organisms typically go through several developmental stages that involve changes not only in structure but also in biochemical and antigenic composition. Some helminth lar-

val stages have little resemblance to the adult stages (for example, those of tapeworms and flukes). Some parasitic protozoa also change greatly during their life history; for example, *Toxoplasma gondii* is an intestinal coccidian in cats but in humans takes on a different form and localizes in deep tissues. Some of these infections can convert from a well – tolerated or asymptomatic condition to life – threatening disease. Many parasitic infections are transmitted from animals to humans (zoonotic infections); the human disease may or may not resemble the disease caused in the lower animal host.

Diagnosis of parasitic infections requires laboratory support, since the signs and symptoms are often nonspecific. A variety of methods and specimens are used for diagnosis. Since the most common parasites are enteric, microscopic examination of fecal specimens is done more often than any other laboratory procedure in the diagnosis of parasitic disease. Culturing has little application in the diagnosis of most parasitic infections, although it has been employed, for example, for *Trichomonas vaginalis* and *Entamoeba histolytica* infections. Immunodiagnostic tests are useful in several infections, including extraintestinal amebiasis, visceral larva migrans, and trichinosis.

New Words

germ [dʒəːm] n. 微生物，细菌

spoilage ['spɔilidʒ] n. 损坏

pneumococcal [ˌnjuːməˌ'kɔkl] adj. 肺炎球菌的

polysaccharide [pɔli'sækəraid] n. 多糖，聚糖，多聚糖

diphtheria [dif'θiəriə] n. 白喉

toxoid ['tɔksɔid] n. 类毒素

cholera ['kɔlərə] n. 霍乱

typhoid [ˈtaifɔid] n. 伤寒症 adj. 伤寒的，斑疹伤寒症的

plague [pleig] n. 鼠疫，瘟疫，麻烦，苦恼，灾祸 vt. 折磨，使苦恼，使得灾祸

antimicrobial [ˌæntimaiˈkrəubiəl] n. 抗菌剂，杀菌剂 adj. 抗菌的

eradicate [iˈrædikeit] v. 根除

Legionella [liːdʒiˈnelə] n. 军团菌

Helicobacter [ˌhelikəˈbæktə] n. 螺菌

peptic [ˈpeptik] adj. 助消化的，胃蛋白酶的 n. 消化器官

venereal [viˈniəriəl] adj. 性病的，性交的

urethritis [ˌjuəriˈθraitis] n. 尿道炎

paradoxical [ˌpærəˈdɔksikəl] adj. 荒谬的

virulence [ˈviruləns] n. 毒力，毒性，恶意

sanitation [sæniˈteiʃən] n. 卫生，卫生设施

susceptibility [səˌseptəˈbiliti] n. 易感性，敏感性，感受性

tuberculosis [tjuˌbəːkjuˈləusis] n. 肺结核

pertussis [pə (ː)ˈtʌsis] n. 百日咳

diarrhea [ˌdaiəˈriə] n. 痢疾，腹泻

epidemiology [ˌepiˌdiːmiˈɔlədʒi] n. 流行病学

ebolavirus [ˈebəlˈvaiərəs] n. 艾博拉病毒

hantavirus [ˈhæntəˈvaiərəs] n. 汉坦病毒

gamut [ˈgæmət] n. 全部，整个范围

virion [ˈvaiəriɔn] n. 病毒（成熟）粒子，病毒体

nuclease [ˈnjuːkliˌeis] n. 核酸酶

progeny [ˈprɔdʒini] n. 子代，子孙，后裔

viremic [ˈvirəmik] adj. 血液的

mycology [maiˈkɔlədʒi] n. 真菌学

fungi [ˈfʌndʒai, ˈfʌŋgai] n. 真菌类 adj. 似真菌的，由真菌引起的

reticulum [riˈtikjuləm] n. 网状组织

mitochondria [ˌmaitə'kɔndriə] n. 线粒体
candidiasis [kændi'daiəsis] n. 念珠菌病
parasitology [ˌpærəsai'tɔlədʒi] n. 寄生虫学
protozoa [prəutəu'zəuə] n. 原虫，原生动物
helminth ['helminθ] n. 寄生虫，蠕虫
arthropod ['aːθrəpɔd] n. 节肢动物 adj. 节肢动物的
innocuous [i'nɔkjuəs] adj. 无害的，无毒的，无伤大雅的
schistosomiasis [ˌʃistəsəu'maiəsis] n. 血吸虫病
malaria [mə'lɛəriə] n. 疟疾，瘴气
cryptosporidiosis [ˌkriptəˌspɔri'ridiəsis] n. 隐孢子虫病
strongyloidiasis [strɔndʒilɔi'daiəsis] n. 类圆线虫病
larval ['laːvəl] adj. 幼虫的，幼虫状态的
tapeworm ['teipwʒːm] n. 绦虫
fluke [fluːk] v. 侥幸成功，意外受挫 n. 意外的挫折，侥幸，倒霉，吸虫
coccidian ['kɔkˌsidiən] n. 球虫 adj. 球虫（的）
fecal ['fiːkəl] adj. 排泄物的，渣滓的，糟粕的
trichinosis [triki'nəusis] n. 旋毛虫病

Phrases and Expressions

pathogenic biology　病原生物学
binary fission　二分裂
tetanus toxoid　破伤风类毒素
antibiotic resistant bacteria　耐药菌
chronic ulcerative colitis　慢性溃疡性结肠炎
Legionnaire's disease　军团病
venereal disease　性病
Ureaplasma urealyticum　解脲脲原体

Chlamydia trachomatis　沙眼衣原体
genetic engineering　基因工程
polymerase chain reaction (PCR)　聚合酶链式反应
hospitalized patients　住院病人
anaerobic condition　厌氧情况，无氧条件
pathogenic bacteria　病原菌
nonpathogenic bacteria　非病原菌
intestinal flora　肠菌类，肠道菌群
rheumatoid arthritis　风湿性关节炎，风湿样关节炎
opportunistic fungal infection　机会性真菌感染
interdisciplinary field　跨学科领域
nematode *Ascaris lumbricoides*　蛔虫
Pneumocystis carinii pneumonia　卡氏肺孢子虫肺炎
life histories　生活史
Toxoplasma gondii　刚地弓形虫
asymptomatic condition　无症状
zoonotic infection　动物源性感染
Trichomonas vaginalis　阴道毛滴虫
Entamoeba histolytica　溶组织阿米巴
extraintestinal amebiasis　肠外阿米巴病
visceral larva migrans　内脏幼虫移行症

Questions

1. How many descriptions are there in the scope of pathogenic biology?
2. How to catalog the bacteria? Please explain for example respectively.
3. What are the characteristics of virus?
4. How about the structure of virus?
5. Please describe the clinical diseases caused by fungi?
6. What are the parasites?

7. How to understand the life histories of parasites?
8. Make a speech or write a summary about the text.

Dialogue

About SARS

John : Professor Sam, would you like to introduce anything about SARS to us?

Professor Sam : Ok, SARS is the abbreviation of Severe Acute Respiratory Syndrome. The SARS epidemic started November 2002 in Guangdong province the People's Republic of China.

Rose : I know Guangdong. It's the southernmost province of mainland PRC. This province is very prosperous and accounts for a large portion of PRC's foreign trade. It is very close to Hong Kong.

Professor Sam : Yes, you are right. SARS is a disease of the upper respiratory tract (nose and throat) that spreads to the lungs. In severe cases the lungs will fill up with fluid and 15% ~ 19% of the people with SARS die from this infection. Early in the epidemic many healthcare workers became ill with SARS because they did not realize that this disease is highly contagious.

John : How does this virus spread?

Professor Sam : good question. SARS spreads by close person – to – person contact. Most cases of SARS involved people who cared for or lived with someone with SARS, or had direct contact with infectious material, for example, tissues containing nasal secretions (snot),

from a person who has SARS. Potential ways in which SARS can be spread include touching the skin of other people or objects that are contaminated with infectious droplets and then touching your eye (s), nose, or mouth. This can happen when someone who is sick with SARS by coughing or sneezing droplets onto themselves, other people, or nearby surfaces.

Rose : How many days does it take when a person exposed with SARS before he becomes ill?

Professor Sam : Around 10 days.

John : What are the symptoms?

Professor Sam : The initial symptoms include a fever of 100.4°F (>38℃) or higher, headache, stiff or achy muscles, a loss of appetite and fatigue. As the virus goes down into the lungs a dry cough may occur and it becomes more difficult for the patient to breath. If really severe the patient will need to be hospitalized, given oxygen and even need a ventilator to help them breath. SARS usually lasts about 2 ~ 3 weeks in most cases. However, severe cases of the illness can last longer.

Rose : Is there any useful drug to cure a person of SARS?

Professor Sam : No specific drug, but some believe that treatment with certain hormone drug will help people with severe infections. Using basic disease isolation techniques developed decades ago it has been shown that this particular disease can be contained.

John : I heard that the causative agent of SARS is coronavirus. Are all the coronavirus so lethal?

Professor Sam : No. There are two other coronaviruses that infect humans. These viruses are RNA – containing viruses and are relatively harmless. They account for around 10% of the common colds people get each year.

Rose : Can you tell us what kind of works the researchers are doing now?

Professor Sam : Yes, that's what I'm going to mention. Many researchers are working on developing laboratory assays to speed diagnosis of SARS. Others are working on potential vaccines and drugs that could be useful in treating this viral infection.

John and Rose : Thank you for your introduction, Professor Sam. We learn a lot today.

Professor Sam : You are welcome.

Reading Material

Infectious Diseases

The record of human suffering and death caused by smallpox, cholera, typhus, dysentery, malaria, etc. establishes the eminence of the infectious diseases. Despite the outstanding successes in control afforded by improved sanitation, immunization, and antimicrobial therapy, the infectious diseases continue to be a common and significant problem of modern medicine. The most common disease of mankind, the common cold, is an infectious disease, as is the feared modern disease AIDS. Some chronic neurological diseases that were thought formerly to be degenerative diseases have proven to be infectious. There is little doubt that the future will continue to reveal the in-

fectious diseases as major medical problems.

In the study and care of patients with infectious disease, physicians use some terms that are not easy to define precisely. A definition of infection as growth of a microorganism in an animal with any resulting host response will include essentially all of the infectious diseases of humans. Many of the body surfaces of humans that communicate with the external environment (eg. the skin and the gastrointestinal and respiratory tracts) support a normal flora, but these microorganisms usually do not invade and cause disease. Under the right circumstances, however, elements of the flora can invade and produce an infection.

A number of other terms are commonly used in describing the infectious diseases. Pathology refers to the abnormality induced by an infection, and pathogenesis to the events producing the pathology. A pathogenic microorganism is a microbe that can cause pathology. Disease refers to the existence of pathology and an infectious disease is a disease caused by a microorganism. Virulence is a term referring to the power of a microbe to produce disease in a particular host. For example, a microorganism may be avirulent for a normal host and highly virulent for an immunosuppressed host. Immunity refers to the degree of resistance of the host for a particular microbe. Finally, it must be appreciated that the occurrence of an infectious disease in a human is a dynamic process that represents a host - parasite interaction. The parasite attempts to multiply and the host defenses seek to control this effort. The task of the physician is to recognize that such a process accounts for the patient's problem and to intervene for the benefit of the patient.

The infectious diseases are usually characterized by the dominant organ system involved. This classification is useful as a guide in ap-

proaching patients. For example, patients do not present complaining of pneumococcal pneumonia; patients present complaining of fever, cough, and chest pain. The physician localizes the disease to the chest (respiratory infection) and then proceeds to develop data proving the presence of a pneumonia caused by the pneumococcus. Thus, we classify infections as respiratory infections, gastrointestinal infections, genitourinary infections, nervous system infections, skin and soft tissue infections, bone and joint infections, cardiovascular infections, and generalized (disseminated) infections.

参考译文

课　文

病原生物学

病原生物学包括的范围很广，医学微生学与寄生虫学均属于其范畴。其中，医学微生物学又包括细菌学、病毒学、真菌学等病原微生物学的许多相关分支学科。

细菌学简介

细菌是单细胞微生物，没有核膜，代谢活跃，二分裂法增殖。在医学上它们是引起疾病的主要原因。细菌学的发展来自于医师为了检验和应用疾病的微生物理论的需要，也来自于与食品和酒的防腐有关的经济上的考虑。

在上个世纪，细菌学的主要进展导致了许多有效疫苗（例如：肺炎球菌多糖疫苗、白喉类毒素和破伤风类毒素）和另外一些效果不太好或者有副作用的疫苗（例如：霍乱、伤寒和鼠疫疫苗）的发展。另一个主要进展是抗生素的发现。这些抗菌的物质虽然没有将细菌性疾病根除，但是它们是有效的治疗手

段。它们的效力由于抗生素耐药性细菌的出现而减弱（现在是一个重要的医疗管理问题）。

大多数现在已知的具有细菌学病因的疾病其实早在几百年前就已有所认识。有一些在古老的中医文献记载中描述为具有传染性的，比在 1677 年第一个描述细菌的列文虎克早数个世纪。仍有一些疾病（例如：慢性溃疡性结肠炎）据一些研究者认为是由细菌引起的，但是一直鉴定不出致病菌。有时，以前不认识的一些疾病竟然与一个新的菌群有关。一个例子是军团病，一种急性呼吸道感染，就是由以前未知的军团菌引起的。同样，一种新认识的病原菌 - 螺旋菌，在消化系统疾病中具有重要作用。另一个重要的例子是，在性病的病因学研究中，发现至少 50% 的尿道炎男性病例与解脲脲原体或沙眼衣原体有关。

由基因工程产生的重组细菌在细菌学研究中具有巨大的用途，而且还可生产用于科学研究和治疗疾病的稀有生物分子（例如：干扰素）。抗生素耐药基因，尽管对临床医生来说是一个问题，但却是进行基因工程所不可或缺的标记。基因探针和聚合酶链式反应对快速鉴定病人标本中的病原菌非常有用。病原菌的基因操作仍旧是确定毒力机制所不可缺少的。随着更多保护性蛋白抗原的鉴定、克隆和测序，将会构建比现在所应用的疫苗更好的重组细菌疫苗。

在发达国家，有记录的住院病人感染 90% 是由细菌引起的。这些病例可能仅反映了发生在普通人群中细菌感染实际数字中的一小部分，通常只是一些严重病例。在发展中国家，许多细菌感染常常对居民的健康产生灾难性的后果。营养不良、寄生虫感染以及卫生状况差是导致这些国家的居民对病原菌易感性增加的因素。据世界卫生组织估计，每年有 3 百万人死于肺结核，50 万人死于百日咳，2.5 万人死于伤寒。由细菌引起的腹泻性疾病，每年可使 5 百万人死亡，是位于心血管疾病之后的第二大死亡病因。

许多细菌性疾病可以看成是机体对细菌的适应失败，因为适应良好的寄生物在其宿主体内生存良好，而不引起宿主出现明显损伤。相对来说，适应良好的无毒力微生物可以在特定条件下引起疾病，例如，以超常增多的数量存在、宿主的防御功能受损（例如：艾滋病和化疗期间）及厌氧条件的存在。病原菌仅占细菌种属的一小部分；非致病细菌对人类是有益的（例如：肠道菌群可产生维生素 K），且可参与氮固定、废水处理、食品生产、药物制备和环境生物治理的关键环节。医学微生物学的重点在于研究直接与医学有关的细菌。

病毒学简介

流行病学调查表明，在发达国家，引起非住院治疗急性疾病的最常见原因是病毒感染。在发展中国家，病毒性疾病使死亡率和永久残疾增加，特别是婴儿和儿童。新出现的病毒性疾病，如 HIV、艾博拉病毒和汉坦病毒引起的疾病，时常出现。虽然抗生素可有效控制大多数细菌性感染，但病毒感染却缺乏有效的控制，且对人体健康的威胁显得更加严重。一些数据表明，尽管已经知道许多疾病由病毒引起，但是还有其他一些严重的疾病要加入到此行列中，例如：青少年糖尿病、风湿性关节炎、各种神经系统和免疫系统疾病，以及一些肿瘤。

病毒是微小的亚细胞生物，无法在宿主细胞外进行复制（胞内专性寄生物）。成熟病毒（病毒体）只包含一种核酸（RNA 或 DNA），最简单的病毒在核酸外仅有一层保护性蛋白外壳。核酸包含病毒在宿主细胞中复制所需的遗传信息。蛋白外壳有两个主要功能：首先，保护核酸免遭胞外物质例如核酸酶的降解；其次，有助于病毒对宿主细胞膜的粘附，因为宿主细胞膜的负电荷对裸露的核酸具有排斥作用。一旦病毒基因组穿入并感染宿主细胞，病毒的复制就主要依靠宿主的能量和合成机制。

病毒的不同成分在细胞内分别合成，然后组装形成成熟的颗

粒。这种复制的装配形式是病毒特有的，与其他小的专性胞内寄生物截然不同。病毒的基本结构允许其同时具有适应性和选择性。许多病毒基因组的适应性表现在，实验条件下，一旦其穿过细胞膜，几乎在所有的细胞内病毒都可以进行复制。另一方面，完整的病毒所具有的选择性，使得大多数病毒体只能感染特定的细胞类型。这种选择性很大程度上是因为核酸的侵入通常需要衣壳粘附在细胞膜上的特定反应，以及一些特殊的胞内成分。

病毒与其他微生物的不同之处在于其对宿主细胞的强依赖性。既然病毒必须在宿主细胞中生长，因此在研究病原学、流行病学、宿主防御或者治疗时，必须将它们一起考虑。

病毒定位在胞内，可以保护病毒免遭宿主的免疫攻击。与此同时，胞内定位使得病毒易受攻击，因为它完全依赖于宿主细胞的合成机制，病毒感染所带来的微小理化变化，诸如炎症、发热、循环改变及干扰素的产生，都可以改变这种合成机制。

掌握病毒入侵、胞内复制和脱离宿主的病原学机制对于正确诊断和治疗病毒性疾病，及防止其在环境中扩散是十分关键的。利用含抗体的免疫球蛋白进行有效治疗，需要知道病毒何时对抗体敏感（例如，病毒在血液中的扩散），何时病毒到达抗体很难奏效的靶器官。许多成功疫苗的研制都基于对发病机制和免疫防御知识的了解。利用干扰素进行治疗时也需要考虑这些问题。

真菌学简介

真菌是真核细胞，象动、植物细胞一样具有核膜包围的细胞核、坚硬的细胞壁、内质网和线粒体。这些结构与细菌完全不同。在已知的约 70，000 种真菌中，约有 300 种可以感染人体。健康人感染真菌一般不太严重，但少数几种危及生命的真菌疾病非常重要。由于抗菌药和免疫抑制剂的应用，真菌病越来越成为一个难题。正常菌群发生改变或者免疫防御机制受损（如艾滋病患者）的个体比健康人更容易出现真菌的机会性感染，比如

念珠菌病。因此，机会性真菌病原体在医学微生物学中的重要性越来越突出。

宿主针对真菌的防御与针对细菌性疾病的防御相似，但是细胞介导的免疫尤其重要。非特异性免疫和细胞免疫是人体抵抗或消除真菌病原体的最重要方式。

寄生虫学简介

医学寄生虫学通常对三群动物进行研究：寄生原虫、蠕虫及那些可以直接致病或者作为许多病原体载体的节肢动物。尽管寄生虫学起源于动物学，今天它已是一个交叉学科，受到微生物学、免疫学、生物化学和其他生命科学的很大影响。

受寄生虫感染的人数以万计，轻者无症状，重者致命。这些寄生虫病仍旧是全世界的主要健康问题（例如，世界上约30%的人受到蛔虫的感染。）。近年来，许多寄生虫病的发生有所上升而非下降（例如：血吸虫病、疟疾）。由于艾滋病的流行，一些寄生虫病的重要性有所增加（例如：隐孢子虫病、卡氏肺孢子虫肺炎及粪类圆线虫病）。

单细胞寄生虫（原虫）和多细胞寄生虫（蠕虫、节肢动物）无论在抗原性上还是生化方面都很复杂，它们的生活史和致病机理也同样复杂。在其生活史中，寄生虫一般都经历几个发育阶段，无论是结构、生化还是抗原组成方面都会出现改变。一些蠕虫的幼虫与成虫很少有相似性（如绦虫和吸虫）。一些寄生原虫在其生活史中也有很大的变化，例如，刚地弓形虫是猫小肠内的球虫，但是在人体内呈现不同的形式，可寄生于深部组织中。一些感染的致病变化很大，可以适应良好或者无症状，也可成为致命性疾病。许多寄生虫感染可从动物传播至人（动物源性感染）；人感染后的症状可以与其低等动物宿主相似或不同。

寄生虫的感染需要实验室支持，因为症状和体征常常是非特异的。诊断中要用到各种方法和标本。因为最常见的寄生虫是肠

内寄生，所以诊断寄生虫疾病的最常见方法是粪便样本的显微镜检查。培养的方法尽管有时会用到，例如阴道毛滴虫和溶组织阿米巴感染的诊断，但在诊断大多数寄生虫感染中较少应用。免疫学诊断在一些感染中很有用，包括肠外疾病、内脏幼虫移行症和旋毛虫病。

对　话

有关 SARS

John：Sam 教授，您能给我们介绍一下有关 SARS 的情况吗？

Sam 教授：好的，SARS 是严重呼吸道综合征的缩写。SARS 的流行始于 2002 年 11 月，源自中国广东。

Rose：我知道广东，它是中国大陆最南边的一个省。这个省非常繁荣，占中国外贸的很大一部分，离香港很近。

Sam 教授：是的，你说的对。SARS 是一种上呼吸道（鼻和咽）疾病，然后扩展到肺。严重的病例中，肺中充满了液体，而且 15% ~19% 的人会因感染 SARS 而死去。在疾病流行的早期，许多医护人员受到 SARS 的感染而生病，因为他们没有意识到这种疾病是高度传染的。

John：这种病毒是如何传播的？

Sam 教授：这个问题问得好。SARS 是由人与人的密切接触而传播的。许多人是由于护理 SARS 病人，或与 SARS 病人共同生活，或是直接接触 SARS 病人的传染性分泌物，比如含有鼻分泌物（鼻涕）的组织而感染的。SARS 潜在的传播方式包括接触被传染性液滴污染的他人的皮肤或者物品，继而污染自己的眼、鼻或口。这种情况可见于 SARS 病人咳嗽或者擤鼻涕时，污染到自身、其他人或者附近的物品表面。

Rose：从一个人接触 SARS 后至发病需要多少天?

Sam 教授：大约 10 天。

John：有哪些症状呢?

Sam 教授：最初的症状包括发热（华氏 100.4 度，摄氏 38 度，或更高），头痛，肌肉僵硬和酸痛，食欲差，乏力。当病毒下行到肺，会出现干咳，病人呼吸起来会更加困难。严重时必须住院治疗，给氧甚至需要使用呼吸机以帮助病人呼吸。大多数 SARS 病例通常持续 2～3 周，然而，严重的病例会持续时间更长。

Rose：有没有一些有用的药物来治疗 SARS 病人?

Sam 教授：没有特效药物，但是有些人认为使用一些激素类药物可对那些严重患者有所帮助。使用几十年以前发展起来的疾病隔离技术，可以使这个病的传播受到限制。

John：我听说 SARS 的传染源是冠状病毒。是不是所有的冠状病毒都这么致命?

Sam 教授：不是。还有另外两种冠状病毒可以感染人体。这两种病毒是 RNA 病毒，相对无害。每年人们所患普通感冒中有 10% 是由它们引起的。

Rose：您能告诉我们现在研究人员正在做哪些工作吗?

Sam 教授：可以，这正是我要说的。许多研究者正在完善实验室化验方法，以快速诊断 SARS。还有些研究人员正在研制治疗这种病毒性感染的有用的疫苗和药物。

John 和Rose：谢谢您的介绍，Sam 先生。我们今天学到了很多东西。

Sam 教授：不客气。

阅读材料

传染性疾病

人类感染并死于天花、霍乱、伤寒、痢疾和疟疾等的记录，使得传染性疾病倍受重视。尽管在卫生状况的改善、免疫接种以及抗微生物治疗方面已经取得了十分瞩目的成绩，传染性疾病仍然是现代医学共同而重要的问题。人类最常见的疾病，普通感冒，是一种传染性疾病，而可怕的现代疾病艾滋病也是如此。一些慢性的神经性疾病，以前认为是退行性疾病，现已证实是传染性的。毋庸置疑，传染性疾病仍旧是将来主要的医学问题。

在研究和治疗传染病患者的过程中，医师使用了一些不容易准确定义的术语。传染被定义为微生物在动物体内生长，并导致出现宿主反应，其中基本包括了所有人类的传染性疾病。人体所有与外界环境相通的部位表面（例如：皮肤、胃肠道和呼吸道）都有正常菌群生长，但是这些微生物通常不侵入机体引起疾病。然而，在合适的情况下，菌群的成分可以侵入机体并引起感染。

还有许多其他术语在描述传染病时被广泛使用。病理学表现是指由感染而引起的异常状态，发病机理是指导致病理学表现的一系列改变。病原微生物是指可引起病理学变化的微生物。疾病是指病理学现象的存在，而传染病是指由微生物引起的疾病。毒力是指一种微生物在特定宿主体内致病的能力。例如，一种微生物可能对正常宿主无毒力，但是对免疫功能受抑的宿主却有很高的毒力。免疫力是指宿主抵抗特定微生物的能力。最后，必须明白，人体传染病的发生是一种动力学过程，表现为宿主与寄生物之间的相互作用。寄生物试图增殖，而宿主则防御以试图控制其增殖。医师的任务就是认识到疾病是由这种过程引起的，并对其进行干预以使患者康复。

传染病通常以主要器官系统受累为特征，据此进行分类对于前来就诊的患者有指导作用。例如，患者并不会主诉肺炎球菌肺炎，患者只是主诉发热、咳嗽及胸痛。医师将疾病定位在胸部（呼吸道感染），然后积累数据以证实有肺炎球菌引起的肺炎存在。这样，我们将感染分为呼吸道感染、胃肠道感染、泌尿生殖器感染、神经系统感染、皮肤及软组织感染、骨及关节感染、心血管感染及全身感染。

（曲东明）

Unit Nine

Text

Medical Immunology

The term "immune" derives from *immunis* in Latin, originally denoted freedom from kinds of burden, such as exorbitant taxes and levies or military service to the Roman state. Now in medical terms, it means freedom from diseases, is concerned with the recognition and disposal of nonself substances from a host.

Getting immunity depends on well – functional immune system. The immune system is a complex functional system consists of diverse organs, tissues, cell and molecules distributed throughout most of the body. Despite the system's complexity, its components are interrelated and act in a highly coordinated and specific manner when they recognize, eliminate, and remember antigen substances. To accomplish this task, the immune system must distinguish between self and nonself material.

The immune system has three primary functions: establishment of immune defense, immune homeostasis and immune surveillance. To protect against diseases, the function of immune defense and immune homeostasis help to recognize and defend against not only pathogens, but also autoantigens. In some cases, these kinds of immunity can be harmful to the hosts. Allergies and autoimmune diseases are the classical examples of detrimental immune responses. The third major function consists of the recognition and destruction of mutant cells that can become cancerous. The incidence of malignant diseases is much lower than predicted by the frequency of abnormal cell generation. A depressed immune surveillance caused by immunodeficiency diseases or chemotherapy – induced immunosuppression may lead to the appearance of some types of cancer.

Medical Immunology, is the basic medical science that studies the constituent, structure and function of the immune system; the development, consequences of every sorts of immune response; the application to the detection, prevention and treatment of clinical disorders. Although immunology is still a young science, it has become vast and complex. Because knowledge of immunology accumulates so rapidly, it is impossible for even the most dedicated researcher, let alone a student, to be familiar with all the advances in this field. Modern immunology has been penetrating into every sphere of basic and clinical medical science, and has formed many branches, such as immunobiology, immunopathology, immunogenecology, immunopharmacology, immunoneurology, molecular immunology, tumor immunology, transplantation immunology, gerontological immunology and clinical immunology etc. Undoubtedly, the advances of immunology will accelerate modern medical science greatly. And the studies of mechanisms of different pathologic and biological process,

furthermore, corresponding clinical intervening methods depend on the progress of immunological theory and technology.

New Words

homeostasis [ˌhəumiəu'steisis] n. 动态平衡；（社会群体的）自我平衡，内稳定

surveillance [sə:'veiləns] n. 监视，监督

pathogen ['pæθədʒ（ə）n] n. 病菌，病原体

allergy ['ælədʒi] n. 过敏，过敏反应

detrimental [ˌdetri'mentl] adj. 有害的

mutant ['mju:tənt] n. 突变

malignant [mə'lignənt] adj. 恶性的

gerontological [ˌdʒerən'tɔlədʒikl] adj. 老年医学的

Phrases and Expressions

exorbitant taxes and levies　苛捐杂税

military service　兵役

nonself substance　异己成分

immune defense　免疫防御

immune homeostasis　免疫自稳

immune surveillance　免疫监视

autoimmune disease　自身免疫性疾病

immunodeficiency diseases　免疫缺陷病

immunosuppression　免疫抑制

Questions

1. What does the term "immune" mean?
2. Does "immune" always help human beings clear nonself material out?

3. What are the purposes of medical immunology?
4. How to describe the immune system's functions of healthy individual?
5. How to understand the role of medical immunology in basic and clinic medical science?
6. Make a speech or write a summary about the text.

Dialogue

1. About Immunolabelling Technology

Teacher : In our last experiment class, I introduced a common – used clinical test which can detect antigen – antibody reaction. Do you remember it?

Students : Is it ELISA (enzyme linked immunosorbent assay)?

Teacher : Yes. It is one typical example of immunolabelling technology. But there are also other methods, who knows?

Student 1 : The antigen or antibody can be labelled by fluorscences.

Student 2 : Some kinds of radiated material too.

Teacher : Very good. Till now, there are so many immunolabelling methods, such as immunofluorescence, enzyme immunoassay, radioimmunoassay, western blotting and so on.

Students : These methods can detect unknown antigen or antibody. But, how can we choose properly?

Teacher : Good question. This related to the gold standard of laboratory method. So we must think of so called 5S principle at least: specificity, sensitivity, simplicity, safety, saving.

Students : That is to say, every method has its advantages and disadvantages. So we should ponder totally according to different

experimental purpose and condition to decide on proper method.

Teacher : Correctly. Then I'll screen the characteristics of every label method. Please analyze which is the best relatively?

2. Allergy

...

Patient : Many little red pimples appeared several days ago.

Doctor : Where were they mainly?

Patient : Hands, forearms, some on the neck.

Doctor : Come on, let me see. Are they itching?

Patient : A little, but not seriously.

Doctor : Did you take any medicine recently?

Patient : I had a cold, and have taken sulphanilamide for more than one week.

Doctor : Did you ever have history of allergy caused by medicine?

Patient : Yes. I had an allergy history of Penicillin. But I never took sulpha medicine before.

Doctor : This time, you may be hypersensitive caused by it.

Patient : Oh. Is it serious?

Doctor : No, it isn't. But you must stop taking it immediately. And I'll prescribe you a kind of anti – allergy medicine, meanwhile you should keep watching on the change of pimples. Usually it will disappear gradually. Please remember not to take sulpha medicine again.

Patient : Ok. Thanks a lot.

Reading Material

1. How to Gain the Immunity?

Initially, the term "immunity" only implied resistance to infective disease, because immunology began through efforts to understand and to intervene in states of diseases, for example, smallpox, cholera, anthrax and so on. Contemporary immunologists investigate all aspects of the immune response, so immunity has acquired a much broader meaning.

Innate immunity (also called natural, nonspecific immunity) operates during the early phases of an immune response. It serves as the first barrier line of defense and includes both external and internal system. External mechanisms prevent the penetration of pathogens into host tissues. Intact skin holds back the invasion of most pathogenic microorganism, and also secretes lactic acid, fatty acids that act as bacteriostatic agents by lowering skin pH. Tears protect the eye by providing a washing action, and also contain a hydrolytic enzyme against gram – positive bacteria called lysozyme. If pathogens are inhaled, mucus and the ciliated epithelium of the respiratory tract act as filters. If pathogens are swallowed, mucus in the digestive tract prevents penetration into cells. The low stomach pH kills organisms, and the normal flora of lower intestine inhibits the attachment of pathogens. If a pathogen breeches the external innate defenses, internal mechanisms provide protection. Physiologic barriers offer inhospitable environments, including high body temperature, high oxygen concentrations. Microorganisms themselves also can activate complement proteins that mediate cell lysis. Virally infected cells release interferons, which interfere with the infection of neighboring cells by the viru-

ses. Inflammation involves increased blood flow to the site of injury and increased permeability of the vascular endothelium to allow access of leukocytes and serum components to the tissues. Phagocytosis, which can trigger inflammation, uses "professional" phagocytes (monocytes, macrophages, and polymorphonuclear leukocytes) to engulf and remove foreign materials.

Adaptive immunity (also called acquired, specific immunity) develops during a host's lifetime and is based partly on the host's experiences called immunization. It is the surveillance mechanism of vertebrates that specifically recognizes foreign antigens and selectively eliminates them, and on reencountering the antigen has an enhanced response. Functionally, T cells are responsible for cell – mediated immunity and regulation of the immune response, while B cells are responsible for antibody – mediated humoral immunity. The former protects against intracellular parasites, such as viruses, and is important in the rejection of organ transplants and tumor cells. TH cells and macrophages release cytokines, Tc cells lyse target cells. The later protects against circulating extracellular antigens such as bacteria, exotoxins, and viruses in extracellular phase.

Humoral and cell – mediated adaptive immunity can each be divided into active and passive immunity. Active immunity is acquired gradually (5 to 14 days after antigen exposure), lasts for years, and is highly protective. Passive immunity lasts for days to months, has low to moderate protective effectiveness, and does not develop memory in the recipient. Both can be further subdivided into natural and artificial forms. If an individual is exposed to foreign substances naturally through the environment, rather than by immunization with a vaccine, that individual acquires the natural rather than the artificial form of active immunity. In passive immunity, an individual has

acquired immunity mediated by antibodies or sensitized T cells. The passage of antibodies from mother to the fetus across the placenta or to the infant through the colostrums is a form of natural passive acquired immunity. Artificial passive acquired immunity occurs when performed antibodies or immune cells are given to a nonimmune individual such as gamma globulin injections for diseases.

2. Cytotoxicity may be Signalled via Fas or TNF Receptor on a Target Cell

Cytotoxic T cells signal to their targets using members of the TNF recrptor group of molecules. These include Fas (CD95) and the type 1 TNF receptor, TNFR - 1, which are widely distributed in the body. Other members of group are CD30 and CD40 which are involved in lymphocyte differentiation. The ligand for Fas (FasL) is expressed on mature $CD4^+$ and $CD8^+$ T cells after activation. Ligation of Fas induces trimerization of the Fas molecules on the cell surface, which causes them to associate with a transducing molecule which recruits and activates caspases 8 or 10. Note that cell killing mediated by Fas also occurs as part of the normal processes of lymphocyte selection, during development. For cytotoxic lymphocytes which lack granules the Fas pathway is thought to be the principle means of signaling to the target.

Most $CD8^+$ Tc cells, NK cells (and macrophages) have vesicles containing TNF and lymphotoxin which can be released onto a target cell. TNF acts in a very similar way to the Fas ligand. It causes trimerization of the TNFR - 1 so that the receptor associates with adaptor proteins which recruit caspases. Both TNFR - 1 and Fas contain intracytoplasmic domains (death domains) which are found on a number of

proteins involved in cell survivial. Note however that a different form of TNF receptor, TNFR－2, lacks these intracytoplasmic segments and therefore does not transducer signals for apoptosis.

Activatd caspase 8 can cleave and activate other caspases, in addition to its own direct actions in the pathways of apoptosis.

3. Tumors Show Multiple Mechanisms for Evading Immune Responses

Because spontaneous tumors grow and kill the host, many tumors must escape the host immune response. Many mechanisms have been proposed. The most obvious is that the tumor is non－immunogenic. This might be because potential tumor antigens are lacking, but, as described earlier, increasing numbers of antigens recognized by cells or antibodies of tumor bearers are now being identified. More likely the weak response to tumors is because they are poor antigen－presenting cells. Even if effector cells are generated, these may recognize and kill the tumor cells with difficulty.

A particularly important escape mechanism is loss of MHC antigens leading to inability to present tumor antigen peptides. More than 50% of tumors may lose one or more MHC class Ⅰ alleles and sometimes all class Ⅰ. A variety of molecular mechanisms has been identified, including mutations in β_2 microglobulin and peptide transporters. The common occurrence of MHC loss in tumors strongly suggests that there is selection for it, presumably by cytotoxic T cells.

Induction of immune responses requires co－stimuli, as do optimal function of effector cells. The CD80 (B7) and CD40 molecules, present on specialized APC, are now known to be key co－stimuli acting via their counter－receptors CD28 and CD40L on the T－cell

surface. Experimentally, presentation of MHC – peptide antigen complexes to the T – cell receptor in the absence of CD80 co – stimulation may lead to anergy, and there is evidence that TILs may sometimes be anergic. This effect may be part of a more general defect in immune responsiveness in cancor patients, because even peripheral blood T cells of tumor patients frequently show defective T – cell receptor signaling in vitro.

Tumor cells may also lack other molecules required for adhesion of lymphocytes such as LFA – 1, LFA – 3 or ICAM – 1, or they may express molecules such as mucins, which can be anti – adhesive. They may also secrete immuno – suppressive cytokines such as transforming growth factor – β (TGF – β) and vascular endothelial growth factor (VEGF).

参考译文

课　文

医学免疫学

术语“免疫”源自拉丁语 *immunis*，原义为免除罗马统治时期的苛捐杂税或兵役。而在现代医学术语中，其含义为免除疾病，即识别并自机体排除异己成分。

免疫力的获得有赖于功能完备的免疫系统。免疫系统是由各种几乎遍布全身的器官、组织、细胞及分子组成的复杂功能系统，但其组成成分相互联系，紧密协调，在识别、清除抗原及产生记忆过程中具有特异性。为了完成其功能，免疫系统必须能够识别“非己”及“异己“成分。

免疫系统具有三大功能：免疫防御、免疫自稳、免疫监视。为了使机体免患疾病，免疫防御及免疫自稳功能不仅可以帮助机

体识别和抵御病原体的侵害，还有助于自身抗原的识别及排除。有时这些免疫功能可对机体造成损伤，过敏反应及自身免疫性疾病就是典型的例子。第三大功能是识别并破坏可转变为癌症的突变细胞，因而，恶性疾病的发病率要比按照异常细胞发生率所预测的比率低。免疫缺陷性疾病或化疗后免疫功能低下所引起的免疫监视功能抑制，可导致一些肿瘤的发生。

医学免疫学是一门研究免疫系统的组成、结构及功能，各种免疫应答的发生发展，及其在临床疾病的检测、预防、治疗中应用的基础学科。虽然免疫学仍是一门年轻的学科，但其涉及内容复杂，领域宽广。由于免疫学知识累积十分迅速，即使是大多数专业研究人员也不可能熟悉此领域内所有的新进展，更何况是一名学生。现代免疫学已经渗透到基础与临床医学的各个领域，并已形成许多分支学科，例如：免疫生物学、免疫病理学、免疫遗传学、免疫药理学、神经免疫学、分子免疫学、肿瘤免疫学、移植免疫学、老年免疫学、临床免疫学等。毫无疑问，免疫学的发展将大力推动现代医学的进步，各种病理及生理过程的机制，以及相应临床干预手段的研究，均有赖于免疫学理论和技术的发展。

对　话

1. 有关免疫标记技术

老师：在上次实验课中，我给大家介绍了一种临床上常用的检测抗原抗体反应的实验，还记得是什么吗？

学生：酶联免疫吸附实验？

老师：对。它是免疫标记技术中的一个典型例子，但还有其他标记方法，大家知道吗？

学生 1：可用荧光素标记抗原或抗体。

学生 2：还可用各种放射性物质标记。

老师：对。到目前为止，有各种免疫标记方法，例如免疫荧光标

记技术、免疫酶标记技术、放射性免疫标记技术、Western 印迹等。

学生： 这些方法都可以检测未知抗原或抗体，但在实际工作中如何合理选择使用呢？

老师： 这个问题问得好。这就涉及到实验方法的金标准选择原则，我们应该考虑到至少 5 个方面，即所谓 5s 标准：特异性（Specificity）、敏感性（Sensitivity）、简便易操作（Simplicity）、安全性（Safety）和省时省钱（Saving）。

学生： 也就是说，每种方法都有优缺点，应根据不同的实验目的、条件等综合考虑后，再确定合适的实验方法。

老师： 完全正确。下面我将每一种标记方法的特点打在屏幕上，大家来分析一下哪种方法相对来说最理想。

2. 过敏反应

……

病人： 这几天身上起了些小红疙瘩。

医生： 主要分布在哪些部位？

病人： 手、胳膊，脖子上也有些。

医生： 来，让我看一看。痒吗？

病人： 有一点，但不很厉害。

医生： 最近有没有服用过什么药物？

病人： 前一段时间有点感冒，吃了一个多星期的增效联磺片。

医生： 以前有药物过敏史吗？

病人： 对青霉素有过敏，但没有用过磺胺类药物。

医生： 这次可能是磺胺类药物引起的过敏反应。

病人： 哦，很严重吗？

医生： 不太严重。但应立即停药。我再给你开一种抗过敏的药物，同时密切观察。一般情况下皮疹很快就会消退。切记以后不要再使用磺胺类药物了。

病人：好吧，谢谢！

阅读材料

1. 怎样获得免疫力?

最初，“免疫力”仅指针对传染性疾病的抵抗力，因为免疫学起源于人类对天花、霍乱、炭疽等传染病的认识和防治。现代免疫学家研究有关免疫应答的所有方面，因此，免疫力有了更深广的含义。

固有免疫（又称自然免疫、非特异性免疫）发生在免疫应答的早期，是机体的第一道防御屏障，包括内部和外部系统。外部固有免疫可阻止病原体进入宿主体内组织。完整的皮肤可以阻断大多数病原微生物的入侵，还可分泌乳酸、脂肪酸，通过降低皮肤表面 pH 值而发挥抑菌作用。眼泪可以通过冲刷作用保护眼睛，并且还含有一种称为溶菌酶的水解酶，可杀死 G^+ 菌。如果病原体被吸入体内，呼吸道粘膜及纤毛上皮细胞就可以发挥滤过作用。如果病原体被吞入体内，消化道粘膜可防止病原体进入细胞内。胃中的低 pH 值可使病原微生物死亡，小肠中的正常菌群可抑制病原菌的粘附。若病原体突破了外部固有免疫防御系统，内部防御系统将发挥保护作用。体内物理屏障将使内部环境不适合细菌生长，包括体温及氧浓度的升高。病原微生物本身也可以激活补体从而介导细胞裂解。病毒感染的细胞可以释放干扰素，阻碍病毒感染相邻的正常细胞。炎症可导致局部血流加速，血管内皮细胞通透性增加，进而白细胞及血清成分到达局部损伤部位。吞噬作用可激发炎症，利用“专职”吞噬细胞（单核细胞、巨噬细胞、多形核白细胞）吞噬、消灭异物。

适应性免疫（又称获得性免疫、特异性免疫）的形成伴随机体的一生，在一定程度上以宿主获得免疫力的经历为基础。它是脊椎动物的一种监视机制，能够特异性识别、选择性清除抗原

性异物，并在再次接触同一种抗原时产生增强的免疫反应。从功能上来说，T 细胞介导细胞免疫及免疫应答的调节，B 细胞与抗体介导体液免疫。细胞免疫主要针对细胞内寄生物，例如：病毒，在器官移植排斥和肿瘤细胞方面亦十分重要。TH 细胞及巨噬细胞可释放细胞因子，Tc 细胞可裂解靶细胞。体液免疫主要针对循环性细胞外抗原，例如：细菌、外毒素、细胞外病毒。

体液及细胞免疫均可划分为主动及被动免疫。主动免疫是逐渐获得的，一般产生于接触抗原后 5～14 天，可持续数年，具有较强的保护作用；被动免疫可持续数日至数月，保护效果较差，且不能产生记忆。主动及被动免疫又可划分为自然、人工两种方式。如果个体不是通过疫苗接种，而是经外界环境自然接触抗原物质，免疫力的获得方式就是自然主动免疫，而不是人工主动免疫。抗体及致敏 T 细胞可介导机体的被动免疫。胎儿经胎盘或婴儿经初乳自母体获得抗体是自然被动免疫的一种方式。通过向无免疫力个体注射抗体（如注射 γ 球蛋白以预防疾病）或免疫细胞，可使机体获得人工被动免疫力。

2. 通过 Fas 或 TNFR 可对靶细胞发挥细胞毒性反应

细胞毒性 T 细胞通过 TNF 受体家族的成员分子与靶细胞之间传递信号，这些分子包括广泛分布于人体的 Fas（CD95）及Ⅰ型 TNF 受体（TNFR－1），其他家族成员还有与淋巴细胞分化有关的 CD30、CD40。Fas 配体（FasL）可表达于成熟的活化 $CD4^+$、$CD8^+$ T 细胞，Fas 的聚集可诱导细胞表面 Fas 分子的三聚体化，导致 Fas 分子与能够活化 caspase 8 或 caspase 10 的信号转导分子发生联系。在细胞发育过程中，由 Fas 介导的细胞杀伤作用也可作为淋巴细胞正常选择过程中的一部分。对于缺乏杀伤颗粒的淋巴细胞而言，Fas 介导的杀伤途径被认为是杀伤靶细胞的主要方式。

大多数 $CD8^+$ Tc、NK、Mφ 内都有许多小囊泡，其内含有可

释放并作用于靶细胞的 TNF 及淋巴毒素。TNF 的杀靶方式与 Fas 配体极相似，它可导致 TNFR－1 的三聚体化，从而使此受体通过连接蛋白募集 caspase。TNFR－1 及 Fas 均含有胞浆内死亡区域，现已在一些与细胞存活有关的蛋白中发现了此区域。但 TNF 的另一种受体 TNFR－2 缺乏这些胞浆内片段，因此不参与凋亡的信号转导。

活化的 caspase 8 能够剪切并激活其他 caspase，另外也可通过自身直接方式介导凋亡。

3. 肿瘤通过多种机制途径逃避免疫应答

一些肿瘤必须能够逃避机体的免疫应答，才能达到自发生长并最终危害宿主生命的目的。目前已经提出了许多肿瘤免疫逃逸机制，其中最显而易见的是肿瘤具有的非免疫原性，即可能是由于肿瘤细胞缺乏有效的肿瘤抗原成分。但是现在越来越多的肿瘤抗原已经被证实，它们可以被肿瘤自身携带的细胞或抗体识别。机体针对肿瘤仅产生极弱的免疫反应，可能是因为抗原递呈细胞功能不全，因此即使产生了免疫效应细胞，也很难有效地识别并杀伤肿瘤细胞。

MHC 抗原缺失是一个极其重要的免疫逃逸机制，从而导致不能有效递呈肿瘤抗原肽。50% 以上的肿瘤缺失一种或多种 MHC－Ⅰ类抗原等位基因，有时全部缺失。现已确定了各种参与肿瘤免疫逃逸的分子机制，包括 β2 微球蛋白及肽转运蛋白的基因突变。肿瘤细胞 MHC 抗原普遍缺失这一现象有力地表明，Tc 很可能与免疫逃逸有关。

和效应细胞发挥功效一样，有效免疫应答的发生也需要协同刺激信号的参与。目前已知表达在特异性抗原递呈细胞表面的 CD80（B7）及 CD40 分子是协同刺激信号中的关键分子，它们分别与 T 细胞表面的 CD28 及 CD40L 发生受体－配体结合。实验证明，在 CD80 协同刺激信号缺如的情况下，MHC－抗原肽－T

细胞受体复合物的存在可导致免疫无能。已有证据表明，TILs有时也可呈免疫无能的状态，这属于肿瘤患者体内普遍存在的免疫应答功能缺陷的一种，因为即使是患者外周血中的T细胞也时常在体外表现为T细胞受体信号的缺陷。

肿瘤细胞也可缺失淋巴细胞粘附所需的其他分子，例如LFA-1、LFA-3、ICAM-1；或者表达抵抗粘附的分子，例如粘蛋白；还可分泌免疫抑制性细胞因子，例如转化生长因子β（TGF-β）、血管内皮生长因子（VEGF）等。

（崔　澈　战庆臣）

Unit Ten

Text

Pathology

Pathology means the study of disease, and begins at the cellular level. When cells of a living human organism are exposed to a noxious physical, chemical or biological agent, they become injured. There are a limited number of different types and mechanisms of injury. The cells generally respond in one of four ways: They get bigger, get smaller, proliferate, or die.

In General Pathology, we study cell adaptations, necrosis, neoplasia, inflammation, vascular, fluid and clotting derangements, and immunologic disease at the cellular and tissue levels. In Systemic Pathology, we study these phenomena at the organ-system level. In both General and Systemic Pathology, we emphasize understanding etiology, pathogenesis, and tissue changes primarily in terms of basic

science (eg. anatomy, biochemistry, physiology and molecular biology) . For example, the common phenomenon is inflammation in the study of pathology. Then, how does inflammation develop? What is typically meant by the term acute inflammation? What are the classic signs of inflammation? And what do these typical signs result from?

Inflammation is a local response to injury. Acute inflammation is that phase of inflammatory response characterized by local edema, hyperemia and polymorphonuclear leukocytosis. The sequence of events is injury to the tissue. This is followed by direct neural stimulation and release of cellular constituents which act as chemical mediators. Next hemodynamic changes occur. These are changes in blood flow and caliber of vessels. There is transient precapillary arteriolar constriction (neurogenic) , followed by dilatation. The result is hyperemia. Permeability changes then follow. These are most pronounced in venular endothelium allowing escape of plasma protein from the blood causing edema. The increased tissue turgor leads to stasis of blood flow. In this particular case, there has been massive outpouring of blood proteins due to marked leakage of the vessels. Outside the vascular space, there has been an activation of the coagulation cascade leading to precipitation of fibrin. The final step is exudation of leukocytes particularly polymorphonuclear leukocytes. The purulent component results from the extravascular accumulation of neutrophils. Inflammatory diseases have viral, bacterial, and fungal causes. Their morphologic patterns are not highly specific. But, uaually the classic signs of inflammation are: Rubor (Redness, result of tissue hyperemia), Tumor (Swelling, result of tissue edema), Calor (Warmth, result of tissue hyperemia), Dolor (Pain, result of tissue turgor, plus action of liberated intracellular amines, enzymes, potassium and blood kinins) and Functio laesa (Dysfunction, due to

all of the above) . And, the major categories of mediators of the inflammatory response and the important mediators respectively were: (1) Vasoactive amines, including histamines and serotonin; (2) Plasma proteases, consisting of three interrelated systems: the kinin system, the complement system, and the clotting system; (3) Arachidonic acid metabolites, namely prostaglandins and leukotrines; (4) Products of neutrophils, including cationic proteins, acid proteases and neutral proteases; (5) Products of monocytes and macrophage, including enzymes, lymphokines, monokines, and other cytokines; (6) Oxygen derived free radicals; (7) Platelet activating factor.

The practice and learning of pathology require a keen interest and a whole – hearted commitment if we are to satisfy the great demands imposed on our specialty by the rapid progress of modern science. Meanwhile, in Clinical medicine, you will understand further how disease affects humans as living beings, with social and psychological consequences of illness.

New Words

noxious ['nɔkʃəs] adj. 有害的

proliferate [prəu'lifəreit] v. 增生扩散

neoplasia ['ni (:) əu'pleiʒiə] n. 瘤形成

hyperemia [ˌhaipə (:)'ri (:) miə] n. 充血

hemodynamic [ˌhi:məudai'næmik] adj. 血液动力学的

caliber ['kælibə (r)] n. 口径，器量

arteriolar [a:ˌtiəri'əulə] adj. 小动脉的

turgor ['tə:gə] n. 细胞（组织）的膨胀，肿胀

stasis ['steisis] n. 停滞，郁积

fibrin ['faibrin] n. （血）纤维蛋白，（血）纤维
exudation [ˌeksju:'deiʃən] n. 渗出液，渗出，分泌
purulent ['pjʊərʊlənt] adj. 脓的，含脓的
rubor ['ru:bə（r）] n. （发炎、毛细血管扩大时）皮肤的红色
calor ['kælə（r）] n. 灼热
dolor ['dəulə]（=dolour）n. 悲哀，忧伤，痛苦
potassium [pə'tæsjəm] n. 钾（19 号元素，符号 K）
kinin ['kainin] n. 激肽
histamine ['histəmi:n] n. 组胺
serotonin [ˌsiərə'təunin] n. 含于血液中的复合胺
metabolite [mi:'tæbəlait] n. 代谢物
prostaglandin [ˌprɔstə'glændin] n. 前列腺素
leukotrine [ˌlju:kə'trin] n. 白细胞三烯

Phrases and Expressions

General Pathology　普通病理学
Systemic Pathology　系统病理学
inflammatory response　炎症反应
local edema　局部水肿
polymorphonuclear leukocytosis　分叶核白细胞增多
chemical mediator　化学介质
plasma protein　血浆蛋白
coagulation cascade　凝血级联反应
functio laesa　功能障碍
vasoactive amine　血管活性胺
complement system　补体系统
clotting system　凝血系统
arachidonic acid　花生四烯酸

cationic protein　负离子蛋白质

Questions

1. How does inflammation develop?
2. What is typically meant by the term acute inflammation?
3. What are the classic signs of inflammation? And what do these typical signs result from?
4. How do neutrophils get into the tissue? What is the function of the neutrophils?
5. What is an abscess?
6. Make a speech or write a summary about the text.

Dialogue

About Edema

Teacher : And now, please look at this picture. What's wrong with this person?

Students : Oh, he got a kind of edema on his legs.

Teacher : Ok. Can you say anything about the cause of edema, Tom?

Tom : Edema is excess fluid in the interstitial space or body cavities. The cause of the edema may be a circulation disturbance leading to a transudate or inflammation resulting in an exudate.

Teacher : That's Ok. Where does the edema occur in usually?

Tom : It can occur in the pleural cavities, pericardial cavity, peritoneal cavity, or in the interstitial space of an injured site, namely local edema, like lower extremity edema and throughout the body namely anasarca.

Teacher : But, are all the fluids of edema same or different? Alice,

have a try?

Alice : It seemed like to be different.

Teacher : In detail, please.

Alice : Edema may be a transudate or an exudate. An exudate is an inflammatory extravascular fluid with a high protein concentration, cellular debris, and specific gravity above 1.020. A transudate is extracellular fluid of low protein content and specific gravity of less than 1.012. A transudate occurs with an intact endothelium, and a increasedly outward flux of fluid. This is the typical picture of edema occurring with congestive heart failure or some other circulatory disturbance. In contrast, an exudate results from a significant increase in permeability of the endothelium of blood vessels caused by inflammation leading to an outpouring of protein rich fluid.

Teacher : And then, what are the specific types of exudates of acute inflammation?

Alice : The various types of exudates caused by inflammation are: Serous, thin fluid, relatively low in protein. Fibrinous, is rich in fibrin. Suppurative, is rich in neutrophils and debris. Hemorrhagic, occurs when vessels rupture.

Teacher : Very good. Who can tell me how the neutrophils in blood get into the tissue? What is the function of the neutrophils in inflammation, Bob?

Bob : Initially, there is margination of the neutrophils along the surface of the endothelium. This is mediated by various cytokines and adhesion molecules. Next the neutrophils undergo emigration through the endothelial functions of the microvasculature into the interstitial space. The process is driven by chemotaxis which is the unidirectional migration of white blood cells toward

chemical attractants released by the damaged tissue. Aggregation of leukocytes then occurs and results in the accumulation of white blood cells at the site of injury. Accumulated white blood cells including neutrophils and macrophages, then become activated and undertake phagocytosis of the damaged tissue constituents.

Teacher: Great! Now, let's turn to another issue …

Reading Material

1. Alteration of Cytochrome Oxidase Subunit I Labeling is Associated with Severe Mitochondriopathy in NRTI – related Hepatotoxicity in HIV Patients

Liver mitochondrial toxicity induced by nucleoside reverse transcriptase inhibitors (NRTI) in human immunodeficiency virus (HIV) patients has been associated with a wide range of liver involvement ranging from low – grade hepatotoxicity, asymptomatic lactacidemia to severe liver insufficiency, with massive steatosis and life – threatening lactic acidosis. Considerable efforts have been made in the last few years to establish clinical guidelines to avoid life – threatening NRTI – associated lactic acidosis. However, the important issue of low – grade NRTI – associated hepatotoxicity still needs to be unravelled since its natural history is largely unknown. We have recently reported a series of 13 monoinfected HIV patients with low – grade NRTI – associated toxicity. Our results outlined the heterogeneity of NRTI – induced hepatotoxicity and raised the question of its diagnosis. The present

study evaluates the expression of cytochrome oxidase (COX) subunits I and IV, encoded by mitochondrial and nuclear DNA, respectively, in NRTI hepatotoxicity. The aim of our study was to compare the detection rate of mitochondrial abnormalities of immunohistochemistry for COX subunit I with electron microscopy. COX subunit I and IV labeling was performed together with light microscopy and ultrastructural analysis in series of 55 liver biopsies from HIV monoinfected and HIV – hepatitis C virus coinfected patients. Clinical data were also recorded. Our major findings were: (1) decreased COX subunit I labeling is associated with severe ultrastructural mitochondrial alterations and may represent overt NRTI – induced mitochondrial cytopathy; (2) mild ultrastructural damage associated with normal COX subunit I labeling is of unknown clinical significance. The results of the study suggest that COX subunit I labeling may be a valuable tool for the diagnosis of mitochondrial liver disease in HIV patients.

2. Squamous Cell Carcinoma of the Upper Respiratory Tract

Squamous cell carcinoma is the most common primary malignant tumor of the upper respiratory tract. Although the nasal cavity and the paranasal sinuses are lined by columnar pseudostratified ciliated epithelium., the squamous carcinoma predominates in these areas. Some carcinomas in the nasal cavity are of a more transitional type and show slight or no evidence of keratinization. Squamous cell carcinoma of the maxillary sinus is particularly treacherous because: (1) Metastases of squamous cell carcinoma from maxillary sinuses are more common than fron other sinuses and from the nasal cavity. (2) Tumors developing in the floor of the sinus readily penetrate the thin cortical bone of the

alveolar ridge and involve the loose vascular cancellous bone. (3) Tumors that originate in the upper portion of the sinus can readily penetrate into the orbit and the ethmoid bone.

Carcinoma of the tonsil is usually ulcerated and the borders of the ulcer are raised and hard; the tumor must be differentiated from Vincent's angina and primary syphilis. It is predominantly a tumor of older men and may spread to the faucial pillars, the lateral wall of the oropharynx, and the cervical lymph nodes.

A primary squamous cell carcinoma of the oropharynx is quite rare. It is more often an extension from a tumor of the palate, the faucial pillars, or the hypopharynx.

Squmous cell carcinoma of the larynx is the most common primary malignant tumor of the upper respiratory tree. Several studies indicated that this neoplasm is related to common factors in a large section of population, such as smoking, abuse of alcohol, and ambient factors related to industrial work (welding, smoke, and fumes). Grossly, carcinoma of the larynx can be fungating, infiltrating, or ulcerated. The classic classification of the laryngeal carcinoma divided the neoplasm into two types: the intrinsic and the extrinsic. The intrinsic carcinoma involves the mucosal lining of the larynx and is further subdivided into the following anatomic areas: supraglottic, glottic, and subglottic. Extrinsic (hypopharyngeal) carcinomas grow more rapidly because they do not have natural defenses. They readily extend to all contiguous structures and metastasize to deep cervical lymph nodes (frequently this is the first symptom). Intrinsic carcinoma of the larynx is usually a well – differentiated tumor that grows slowly and remains superficial for a prolonged period. However, when the tumor starts to infiltrate, it progresses rapidly even though the metastasis appears later.

Squamous cell carcinoma of the tongue is quite frequent; it is predominantly a disease of elderly men (3:1). Important underlying and predisposing factors are poor oral hygiene, the use of tobacco and alcohol, and a history of syphilis. These factors have as a common denominator chronic irritation of mucosa, which later develops into leukoplakia, precancerous dysplasia, then carcinoma. Grossly the lesion appears as a superficial ulcer covered by a purulent membrane; the surrounding mucosa frequently is leukoplakic. The tumor frequently metastasizes to cervical lymph nodes and infiltrates surrounding structures, especially if a carcinoma arises from the base of tongue. Visceral metastases are rare.

3. **Primary Tuberculosis**

The primary complex represents the morphologic expression of tuberculous infection in an individual never infected previously. The primary complex may occur in either lung and consists of a parenchymal lesion (round, gray nodule measuring 1 to 2 cm, usually subpleural, and often located near the fissure between the upper and lower lobes) and a lymphatic component with involvement of the draining lymph nodes. The two lesions may appear connected by a series of tubercles along the draining lymphatic vessels.

The reaction to the first infection is mostly proliferative in type, with phagocytosis, intracellular lysis of mycobacteria, and active proliferation and differentiation of host cells determined by various mycobacterial cellular components. Specifically, macrophages, epithelioid cells, and eventually multinucleated giant cells are formed, and there is active proliferation of lymphocytes. These cellular elements in various combinations and in conjunction with caseous necrosis (direct-

ly caused by the mycobacteria) and the reparative phenomena of reabsorption and fibrosis (operated by the host) determine the histologic appearance of the disease.

The elementary lesion is the tubercle, which forms about 15 days after infection and is preceded by a stage characterized by nonspecific inflammation. The tubercle is more or less spherical in shape and consists of a central area of caseation (a constant feature in the primary complex) surrounded by lymphocytes, plasma cells, palisading epithelioid cells, and, at a later stage, Langhans" giant cells. Chara cteristically, no exudative reaction is present surrounding the lesion. The usual outcome is healing with fibrosis and calcification. Cavitation is a very rare occurrence. Serofibrinous pleuritis may occur locally with accumulation of a moderate effusion. The involved lymph nodes are often much larger than the parenchymal focus and take longer to resolve. Histologically, the same features are observed as in the parenchymal localization.

Morphologic variants of the primary complex may be determined either by hyperergic reactivity of the host or by massive bacterial inoculum. A very large inoculum of mycobacteria may result in massive caseous necrosis, with formation of a giant primary lesion (up to 7 or 8 cm in diameter). Rarely, caseation may involve an entire lobe of the lung.

In infants, children, or immunosuppressed adults, the primary complex may not regress but rather spread locally or systemically. Complications may be listed as follows: (1) Formation of satellite foci in the lung as a result of early local spread. (2) Tuberculous bronchopneumonia, caused by intrabronchial spread following erosion and penetration of caseous material into a bronchus. (3) Miliary tuberculous, characterized by innumberable small, disseminated,

yellow – gray, firm lesions and secondary to erosion and penetration of a large amount of caseous material into a blood vessel.

参考译文

课　文

病理学

病理学即对疾病始于细胞水平的研究。当人体细胞暴露于有害的物理、化学或生物性因素时，就会受到损伤，这种损伤具有几种不同类型和机制。细胞对损伤的反应一般表现为以下四种方式之一：增大、缩小、增殖或死亡。

普通病理学在细胞和组织水平研究细胞适应、坏死、肿瘤形成、炎症、血管障碍、体液和凝血障碍，以及免疫性疾病。系统病理学在器官系统水平研究这些现象。无论在普通病理学还是系统病理学，最初都基于基础学科（例如，解剖学、生物化学、生理学和分子生物学）重点了解病因学、发病机理和组织变化。

例如，病理学研究中最常见的现象是炎症。那么，炎症是如何产生的？急性炎症的典型特点是什么？炎症的典型症状有哪些？这些典型症状是如何产生的？

炎症是机体针对损伤的局部反应。急性炎症是以局部水肿、充血及分叶核白细胞增多为特征的炎症反应阶段。其发生顺序是，损伤发生后产生直接神经刺激和作为化学介质的细胞成分的释放；然后发生血液动力学改变，即血流量和血管口径的变化，表现为毛细血管前小动脉短暂收缩狭窄（神经源性），接着是扩张，结果导致充血，然后发生血管通透性变化。这些大多发生在小静脉内皮，导致血浆蛋白从血液中大量渗出引起水肿，组织肿胀程度的加重导致血流停滞。在这种特定条件下，许多血液蛋白

因血管渗漏而漏出。在血管外间隙，凝血级联反应的活化导致纤维蛋白沉积。最后是白细胞尤其是分叶核白细胞的渗出。中性粒细胞在血管外堆积导致化脓性成分的形成。炎症性疾病的病因有病毒性、细菌性和真菌性感染。其形态学变化无很高的特异性，但其典型症状一般是：红（赤红，组织充血的结果）、肿（肿胀，组织水肿的结果）、热（温暖，组织充血的结果）、痛（疼痛，组织充盈，以及释放的细胞内胺类物质、酶、钾和血液中激肽作用的结果）、功能障碍（功能不良，由上述所致）。同时，炎症反应的介质主要分类及其中重要的介质分别是：（1）血管活性胺，包括组织胺和5－羟色胺；（2）血浆蛋白酶，包括三个相关系统：激肽系统、补体系统和凝血系统；（3）花生四烯酸代谢产物，即前列腺素和白细胞三烯；（4）中性粒细胞产物，包括阳离子蛋白质、酸性蛋白酶和中性蛋白酶；（5）单核细胞和巨噬细胞产物，包括各种酶类、淋巴因子、单核因子和其他细胞因子；（6）自由基氧；（7）血小板活化因子。

如果想要满足此专业因现代医学飞速发展而出现的最大需求，我们在病理学的实践和学习中就需要具有强烈的兴趣和全身心的投入。同时，在临床医学中，需要进一步了解社会和心理因素作用下疾病对人体的影响。

对　话

有关水肿

老师： 现在，请看这张图。这个人怎么了？

学生们： 噢，双下肢水肿。

老师： 对。Tom，你能说说水肿的病因吗？

Tom： 水肿是指过剩的液体存在于细胞间隙或体腔中。水肿的原因是循环受阻，导致漏出液或炎症引起的渗出液形成。

老师： 对。水肿经常发生在什么部位呢？

Tom：可以发生在胸膜腔、心包腔或腹膜腔。或者，在损伤部位的组织间隙，称为局部水肿，比如下肢水肿，或在全体称为全身水肿。

老师：但是，所有水肿产生的液体一样还是不一样？Alice，你试试吧？

Alice：好象不一样。

老师：说详细点儿。

Alice：水肿可以是漏出液或渗出液。渗出液是一种含高蛋白和细胞碎片的炎症性血管外液体，比重大于1.020。漏出液是一种低蛋白细胞外液，比重低于1.012 。漏出液产生时，血管内皮完整，血管内液体压力增高，这是充血性心力衰竭或其他循环受阻性疾病发生时的典型现象。与之相比较，渗出液的产生是由于炎症导致血管内皮通透性增加而引起富含蛋白的液体溢出。

老师：那么，急性炎症产生的渗出液都有哪些特殊类型呢？

Alice：炎症性渗出液的不同种类包括：浆液性，为稀薄液体，蛋白量相对较低。纤维素性，富含纤维蛋白。化脓性，富含中性粒细胞和细胞碎片。出血性，当血管破裂时。

老师：不错！谁能告诉我，中性粒细胞是怎样从血液进入到组织的？中性粒细胞在炎症中的作用是什么？

Bob：首先，中性粒细胞沿血管内皮表面边集。这一过程由各种细胞因子和粘附分子介导。然后，中性粒细胞通过微脉管系统的内皮功能进行血细胞渗出进入组织间隙。这一过程受趋化性控制。趋化性是指白细胞向损伤组织释放的化学趋化因子单向迁移。于是，白细胞聚集堆积在损伤部位。聚集的白细胞包括中性粒细胞和巨噬细胞，继而被激活，并吞噬损伤的组织成分。

老师：很好！现在我们转到另一话题……

阅读材料

1. NRTI 相关的肝毒性 的 HIV 患者细胞色素氧化酶亚单位 I 标记的改变与严重线粒体病的关系

HIV 患者因使用核苷反转录酶抑制剂（NRTI）而诱发的肝脏线粒体毒性，与大面积肝脏受累有关，其范围从低度肝中毒，无症状乳酸血症，到出现巨型皮脂腺病和威胁生命的乳酸中毒相关性严重肝功能障碍。在过去几年里，我们做了很多工作，建立临床指导以避免威胁生命的 NRTI 相关性乳酸中毒的发生。但是，由于其自身发展很多是未知的，NRTI 相关性低度肝中毒的重要问题仍有待解答。我们最近报告了一系列 13 例伴有低度 NRTI 毒性的单纯 HIV 感染病人，概括了 NRTI 导致肝中毒的异质性，并提出了它的诊断问题。本研究分析了在 NRTI 性肝中毒患者由线粒体和核 DNA 编码的细胞色素氧化酶（COX）亚单位 I 和 IV 的表达。我们的研究目的是采用电子显微镜术比较线粒体异常时 COX I 的免疫组化表达率。采用光镜和超微结构分析，对 55 例 HIV 单纯感染和合并丙型肝炎病毒感染患者的肝脏切片进行 COX I 和 IV 标记分析。同时我们也记录了临床资料。我们的主要研究结果是：（1）COX I 标记的减少与线粒体超微结构的严重改变有关，可代表已知的 NRTI 诱导的线粒体细胞病变。(2) 正常的 COX I 标记与轻微的超微结构损伤有关，具有未知的临床意义。研究结果表明，COX I 标记可能有助于诊断 HIV 患者的线粒体性肝病。

2. 上呼吸道的鳞状细胞癌

鳞状细胞癌是上呼吸道最常见的原发性恶性肿瘤。虽然鼻腔和鼻窦内衬假复层纤毛柱状上皮，但鳞癌在这些区域仍占主导地位。鼻腔肿瘤更多的是一些过渡类型，表现出轻微角化或并无角化现象。上颌窦鳞状细胞癌尤其可怕，因为：(1) 与鼻腔及其他鼻

窦相比，上颌窦鳞状细胞癌更易发生转移。（2）鼻窦底部肿瘤的发展易于穿透牙槽嵴薄薄的皮质骨，并且还可形成疏松的血管海绵状骨。（3）源于鼻窦上部的肿瘤易于穿入眼眶和筛骨。

扁桃体部位的癌症常呈溃疡性，溃疡的边缘陡而硬，肿瘤分化自 Vincent 咽峡炎和一期梅毒。其发病在老年性肿瘤中占优势，并可浸润至咽腭弓、口咽外侧和颈淋巴结。

口咽部原发性鳞癌很少见，而腭、咽腭弓或喉咽部肿瘤较常见。

喉鳞癌是上呼吸道肿瘤中最常见的原发性恶性肿瘤。一些研究表明，这种肿瘤与大面积人群中常见的致病因素有关，例如：吸烟、酗酒、与工业化有关的环境因素（焊接、烟、汽）。大体来说，喉癌可迅速生长、扩散或呈溃疡性。其按传统分类方法可分为两种：内源性及外源性。内源性喉癌累及喉部粘膜，并可按以下解剖部位进一步分类：声门上、声门、声门下。外源性（咽下部）喉癌生长迅速，因为此处无天然防御，从而易于扩散累及所有附近的结构，并可转移至颈深部淋巴结（这通常是第一体征）。内源性喉癌常常是一种高分化肿瘤，生长缓慢，表浅病变可维持很长时间。但是，一旦当肿瘤开始浸润时，即使转移发生较晚，其发展亦极快。

舌鳞癌很常见，是老年男性的主要疾病（占 1/3）。其重要的患病因素是不良的口腔卫生、吸烟、饮酒和梅毒病史。这些因素作为常见的对粘膜的慢性刺激，最终可发展成为粘膜白斑病、癌前病变，直至癌症。总体来说，其局部病变看似表浅的溃疡，表面覆有一层脓性膜，周围的粘膜通常呈白斑病变。肿瘤常转移至颈淋巴结，并浸润至周围组织，特别是当疾病源自舌根时。内脏转移较罕见。

3. 原发性结核

原发综合征是以往从未感染过结核的个体发生结核性感染后的代表性形态学表现。双肺均可发生，包括一个实质性损害

（圆形、灰色结节，1～2cm，通常位于胸膜下，上、下肺叶裂隙处），及相应受累的引流淋巴结。2 种损害可导致沿着引流淋巴结出现一连串结核结节。

机体对第一次结核菌感染的反应大多为增生型，伴吞噬现象、细胞内分枝杆菌溶解、以及因分枝杆菌成分不同而引起宿主细胞的活性增殖和分化。特别是，巨噬细胞、上皮样细胞以及最终多核巨细胞的形成，还有淋巴细胞的活性增殖。这些不同组分的细胞成分与干酪样坏死（直接由分枝杆菌引起）结合在一起，以及再吸收和纤维化的代偿现象，共同构成了这种疾病的组织学表现。

最初的损伤是在感染后 15 天左右结核结节的出现，由以非特异性炎症为特征的阶段发展而来。结核结节的形状为球形或近似球形，中央区域为干酪样坏死（原发综合征的常见特征），四周浸润有淋巴细胞、浆细胞、平行排列的上皮样细胞，晚期还有朗罕氏细胞。具有特征性的是，在损伤部位无渗出性反应，通常的愈合结局是纤维化和钙化，空洞形成极少发生，浆液纤维蛋白性胸膜炎伴中度渗出可在局部发生。淋巴结的受累面积常大于实质病灶，且愈合需要时间很长。从组织学上来看，受累淋巴结的变化与实质损伤部位相似。

原发综合征形态学上的差异取决于宿主对细菌的过度反应程度及入侵细菌的数量。大量结核杆菌的入侵可导致大面积的干酪样坏死，并形成巨大的原发损伤（直径可达 7～8cm）。累及整个肺叶的干酪样坏死罕见。

在婴幼儿、儿童或处于免疫抑制状态的个体，原发病变不仅不能消退，反而会导致局部或全身扩散。其并发症如下：（1）因早期局部扩散所致肺内卫星灶；（2）支气管扩散引发干酪样物质侵蚀并穿透支气管，导致结核性支气管肺炎；（3）粟粒性肺结核，以不计其数遍布组织的灰黄色小结核结节为特征，形成损伤后大量干酪样物质可侵蚀并穿入血管。

（崔　激　金玉祥）

Unit Eleven

Text

Pharmacology

Pharmacology can be defined as the study of drugs that interact with living systems through chemical processes, especially by binding to regulatory molecules and activating or inhibiting normal body processes.

In the most general sense, a drug may be defined as any substance that brings about a change in biologic function through its chemical actions. In the great majority of cases, the drug molecule interacts with a specific molecule in the biologic system that plays a regulatory role, eg. a receptor molecule. In a very small number of cases, drugs known as chemical antagonists may interact directly with other drugs, while a few drugs (eg. osmotic agents) interact almost exclusively with water molecules. Drugs may be synthesized within the body (eg. hormones) or may be chemicals not synthesized in the body (eg. xenobiotics). Poisons are drugs. Toxins are usually defined as poisons of biologic origin, eg. synthesized by plants or animals, in contrast to inorganic poisons such as lead and arsenic. In order to interact chemically with its receptor, a drug molecule must have the appropriate size, electricalcharge, shape, and atomic composition. Furthermore, a drug is often administered at a location distant from its intended site of action, eg. a pill given orally to relieve a headache. Therefore, a useful drug must have the necessary properties to be transported from

its site of administration to its site of action. Finally, a practical drug should be inactivated or excreted from the body at a reasonable rate so that its actions will be of appropriate duration.

The interactions between a drug and the body are conveniently divided into two classes. The actions of the drug on the body are termed pharmacodynamic processes. These properties determine the group in which the drug is classified and often play the major role in deciding whether that group is appropriate therapy for a particular symptom or disease. The actions of the body on the drug are called pharmacokinetic processes. Pharmacokinetic processes govern the absorption, distribution, and elimination of drugs and are of great practical importance in the choice and administration of a particular drug for a particular patient, eg. one with impaired renal function.

Therapeutic effects of drugs result from their interactions with molecules in the patient. Most drugs act by associating with specific macromolecules in ways that alter the macromolecules' biochemical or biophysical activities. This idea is embodied in the term receptor.

As we have seen, the existence of a specific drug receptor is usually inferred from studying the structure – activity relationship of a group of structurally similar congeners of the drug that mimic or antagonize its effects. Thus, if a series of related agonists exhibits identical relative potencies in producing two distinct effects, it is likely that the two effects are mediated by similar or identical receptor molecules. Thus, studies of the relation between structure and activity of a series of agonists and antagonists can identify a species of receptor that mediates a set of pharmacologic responses.

The goal of therapeutics is to achieve a desired beneficial effect with minimal adverse effects. When a medicine has been selected for a patient, the clinician must determine the dose that most closely

achieves this goal. A rational approach to this objective combines the principles of pharmacokinetics with pharmacodynamics to clarify the dose – effect relationship. Pharmacodynamics governs the concentration – effect part of the interaction, whereas pharmacokinetics deals with the dose – concentration part. The pharmacokinetic processes of absorption, distribution, and elimination determine how rapidly and for how long the drug will appear at the target organ. The pharmacodynamic concepts of maximum response and sensitivity determine the magnitude of the effect at a particular concentration.

Knowing the relationship between drug concentration and effects allows the clinician to take into account the various pathologic and physiologic features of a particular patient that make him or her different from the average individual in responding to a drug.

New Words

pharmacology [ˌfɑːməˈkɔlədʒi] n. 药理学

antagonist [ænˈtægənist] n. 拮抗剂

osmotic [ɔzˈmɔtik] adj. 渗透性的

xenobiotic [ˌzenəʊbaiˈɔtik] n. 异生物，外源物

lead [liːd] n. 铅

arsenic ['ɑːsənik] n. 砷

pharmacodynamic [ˌfɑːməkəʊdaiˈnæmik] adj. 药物效应动力学的，药效动力学的，药效学的

pharmacokinetic [ˌfɑːməkəu.kaiˈnetiks] adj. 药物代谢动力学的，药代动力学的，药动学的

renal ['riːnl] adj. 肾脏的，肾的

congener ['kɔndʒinə] n. 同种的物，同类的人，同属的动、植物

adj. 同种的，同类的

antagonize [æn'tægənaiz] vt. 对抗

agonist ['ægənist] n. 激动剂，激活剂

clarify ['klærifai] v. 澄清，使明白；使（液体等）清洁（不含杂质）

sensitivity ['sensə'tivəti] n. 敏感性

magnitude ['mægnitju:d] n. 大小，量，重要（的程度）

Phrases and Expressions

be defined as 被定义为

electrical charge 电荷

therapeutic effect 疗效

structure – activity relationship 构效关系

pharmacologic response 药理学效应

adverse effect 不良反应

dose – effect relationship 量效关系

target organ 靶器官

Questions

1. Please explain the term "receptor"?
2. How to classify the interaction between drugs and living system?
3. How to understand pharmacokinetics and pharmacodynamics respectively?
4. Can you talk about the principles of drug using?
5. Make a speech or write a summary about the text.

Dialogue

1. Talking about Drugs between Teacher and Student

Student : Professor, would you like to tell us what the basic purposes of therapy are?

Professor : The basic purposes of therapy are to prevent and to cure diseases. If these goals can not be achieved, the secondary therapeutic objectives should be to mitigate and to mollify the progressive, devastating, or disabling nature of diseases by drugs.

Student : Could you tell us what the amount of drug or drugs to be given and the duration of therapy to be instituted depend on?

Professor : Sure. The amount of drug or drugs to be given and the duration of therapy to be instituted depend on the nature of the disease to be treated. For example, an uncomplicated urinary tract infection may be cured with 10 days' treatment with a sulfonamide, whereas a patient with grand mal epilepsy may have to be treated for life with phenytoin or phenobarbital or both.

Student : And what will the successful treatment of diseases depend on?

Professor : The successful treatment of diseases will depend on using drugs, and the drugs should be in sufficient amount to obtain the desirable effects and to avoid the harmful side effects.

Student : How to determinate the method of using different drugs?

Professor : In the past, the therapeutic regimens of numerous drugs, including morphine and cardiac glycosides, were established by empiric observations and by trial and error. Dealing often with naturally occurring drugs, physicians chose the drugs, decided on doses and frequency of administration, noted and recorded the beneficial effects, and adjusted the regimen if toxic reactions had occurred. Nowadays, strict examination and endorsement and experimental judge must be done during the period of drug development and clinical application, because the best effects are expected.

Student : Now I see. Thanks! Professor.

Professor : You are welcome.

2. Where do Drug Biotransformation Occur?

Frank : Do you know where metabolism occurs after drugs are taken into the body?

Tony : Liver?

Frank : Not correct. Almost every tissue has some ability to metabolize drugs, but liver is the principal organ of drug metabolism. Other tissues that display considerable activity include gastrointestinal tract, lungs, skin, and kidneys.

Tony : And then, what is the first – pass effect of drugs?

Frank : Following oral administration, many drugs are absorbed intact from the small intestine and transported first via the portal system to the liver, where they undergo extensive metabolism. This process has been called a first – pass effect. Through interacting with gastric acid, digestive

enzymes, microorganisms in lower gut, some orally administered drugs also can be biotransformed, which are more extensively metabolized than in the liver. Thus, intestinal metabolism may contribute to the overall first – pass effect.

Tony : That is to say, first – pass effects of orally administered drugs may so greatly limit their bioavailability?

Frank : Yes. So, alternative routes of administration must be employed to achieve therapeutically effective blood levels.

Tony : Which substance leads to drug biotransformation in vivo on earth?

Frank : The vast majority of transformations are catalyzed by specific cellular enzymes. At the subcellular level, these enzymes may be located in the membrane, plasma, nuclear envelope and endoplasmic reticulum, mitochondria, lysosomes.

Tony : A considerable change in vivo happened before exerting drug efficacy.

Reading Material

1. Plasma Protein Binding: is it Important?

Plasma protein binding is often mentioned as a factor playing a role in pharmacokinetics, pharmacodynamics, and drug interactions. However, there are no clinically relevant examples of changes in drug disposition or effects that can be clearly ascribed to changes in plasma protein binding. The idea that if a drug is displaced from plasma proteins, it would increase the unbound drug concentration and increase the drug effect, and perhaps, produce toxicity

seems a simple and obvious mechanism. Unfortunately, this simple theory, which is appropriate for a test tube, does not work in the body, which is an open system capable of eliminating unbound drug.

First, a seemingly dramatic change in the unbound fraction from 1% to 10% releases less than 5% of the total amount of drug in the body *into the unbound pool because less than one – third of the drug* in the body is bound to plasma proteins even in the most extreme cases, eg, warfarin. Drug displaced from plasma protein will of course distribute throughout the volume of distribution, so that a 5% increase in the amount of unbound drug in the body produces at most a 5% increase in pharmacologically active unbound drug at the site of action.

Second, when the amount of unbound drug in plasma increases, the rate of elimination will increase (if unbound clearance is unchanged) , and after four half – lives the unbound concentration will return to its previous steady state value.

The clinical importance of plasma protein binding is only to help interpretation of measured drug concentrations. When plasma proteins are lower than normal then total drug concentrations will be lower but unbound concentrations will not be affected.

2. Drug Discovery

During the past 60 years, new drug developments have revolutionized the practice of medicine, converting many once fatal diseases into almost routine therapeutic exercises. One cause of this medical advance has been a fundamental improvement in the means of developing and testing new drugs. This process has been greatly accelerated by new technology, by financial motivation, and by

governmental support of medical research. In most countries, the testing of drugs is now regulated by legislation and closely monitored by governmental agencies.

The first step in the development of a new drug is the discovery or synthesis of a potential new drug molecule. By law, the safety and efficacy of drugs must be defined before they can be marketed. In addition to in vitro studies, most of the biologic effects of the molecule must be characterized in animals before human drug trials can be started. Human testing must then go forward in three conventional phases before the drug can be considered for approval for general use. A fourth phase of data gathering follows after approval for general use.

Enormous costs, from $100 million to over $500 million, are involved in the development of a single successful new drug. These costs include the labor invested in searching for useful new molecules – 5000 ~ 10, 000 may be synthesized for each successful new drug introduced – and the costs of detailed basic and clinical studies and promotion of the ultimate candidate molecule. It is primarily because of the economic investment and risks involved that most new drugs are now developed in the laboratories of pharmaceutical companies. At the same time, the incentives to succeed in drug development are equally enormous. The worldwide market for ethical (prescription) pharmaceuticals in 1991 was estimated. to be $284 billion. Moreover, it has been estimated that during the second half of the 20th century, medications produced by the pharmaceutical industry saved more than 1.5 million lives and $140 billion in the costs of treatment for tuberculosis, poliomyelitis, coronary artery disease, and cerebrovascular disease alone.

Most new drug candidates are identified through one or more of

four approaches: (1) chemical modification of a known molecule; (2) random screening for biologic activity of large numbers of natural products, banks of previously discovered chemical entities, or large libraries of peptides, nucleic acids, or other organic molecules; (3) rational drug design based on an understanding of biologic mechanisms and chemical structure; and, increasingly; (4) biotechnology and cloning using genes to produce larger peptides and proteins. In addition to these efforts, major attention is now being given to the discovery of entirely new targets for drug therapy, eg. the intracellular receptors for second messengers.

3. The Discovery and Development of Recombinant Tissue Plasminogen Activator (rt-PA)

The thrombotic complications of cardiovascular disease are a major cause of death and disability. Use of drugs to dissolve blood clots, however, is relatively recent, emerging only over the last two decades. The only available thrombolytic drugs during the early 1980s were the naturally occurring substances streptokinase (from streptococci) and urokinase (from cultured human renal cells). Uncertainty about their efficacy, the great risk of hemorrhage due to a generalized proteolytic effect of these drugs on key proteins involved in blood clotting, and the lack of clot and fibrin selectivity restricted their use to a few academic centers. Moreover, streptokinase was associated with the significant additional risk of antigenicity and occasionally anaphylaxis. So, a more selective or effective thrombolytic agent could have a dramatic clinical impact. Central to current thrombolytic therapy and a clear example of progress in the use of biotechnology for drug

discovery was the research, development, and marketing of rt – PA.

In 1980 Desire Collen, a Belgian physician and scientist long interested in blood clotting, had begun using a human cell line as a source of a littlestudied naturally occurring fibrin – selective thrombolytic substance. Only traces of it were detectable in the body. While the data were of considerable interest, there appeared to be no practical way to produce enough of this large molecule to effectively characterize or use it. Diane Pennica, a newly hired molecular biologist at the then young California biotechnology company Genentech, heard Collen present his preliminary data at a scientific meeting. Pennica, also new to the field, had just started working on approaches to produce by biotechnology methods – another naturally occurring blood clot dissolving protein, urokinase. As the two scientists discussed how they could collaborate, an idea was bom that was to lead to the first successful clot – busting drug, establish the value of thrombolysis, and jump – start the biotechnology industry.

Collen was searching for thrombolytic drugs that would have improved efficacy and safety and could be manufactured efficiently. The hypothesis was that t – PA, one of the body's endogenous thrombolytic substances, might have an enhanced affinity for fibrin in blood clots compared with its affinity for circulating fibrinogen. The local conversion of plasminogen to the active proteolytic plasmin thus might result in selective lytic activity in preformed clots as the insoluble fibrin was degraded to soluble forms. At the same time, t – PA should have less effect on other clotting – related proteins and therefore fewer adverse effects, especially less risk of bleeding.

Pennica and the Genentech team believed that once they had a reliable source of t – PA for chemical sequencing and a source of the human gene, they could clone the gene and transfer it to a microbial

or animal cell line for large – scale rt – PA production. No one had ever successfully cloned and expressed a protein as large and complex as t – PA.

It took Pennica and colleagues 2 years to determine the genetic code, transfect and express the gene, and complete the initial in vitro studies. Collen, who was now a consultant to Genentech, had meanwhile demonstrated for the first time – in two patients – the clinical thrombolytic efficacy of t – PA from the Bowes cell line.

It took 5 more years for clinical trials and regulatory approval of the recombinant material. In November of 1987, rt – PA received NDA approval, and the utility of rt – PA has been confirmed and extended in numerous large – scale clinical trials. The time from the birth of the idea to drug approval for rt – PA was 7 years – one of the fastest times on record for drug discovery and development.

参考译文

课　文

药理学

药理学是研究通过化学过程，特别是通过与调控分子结合并激活或抑制正常机体反应的过程而与机体相互作用的药物的科学。

通常，药物可以指通过化学反应而改变机体生物功能的任何物质。多数情况下，药物分子与机体内的特殊分子相互作用，这种特殊分子在机体内起调控作用，比如受体分子；少数情况下，药物作为化学拮抗剂与其他药物直接相互作用，一些药物（如渗透性药物）几乎仅与水分子相互作用。药物可以是机体自身合成的（如激素），也可是非自身合成的化学药品（如外源性药

物）。毒物也是药物。毒素通常是生物源性毒物，由植物或动物合成，而石墨和砷等则属无机毒物。为了能与其受体产生化学作用，药物分子必须具有适宜的大小、电荷、形状和原子结构。进而，药物的给药部位通常远离其作用位点，例如缓解头痛的药丸口服给药，因此，一种有效药物必须具备可从给药部位到达作用部位的基本特点。最后，有实用价值的药物应能以合理的速度被灭活或排出体外，只有这样药物才能维持适当的作用时间。

药物与机体间的相互作用可分为两大类：药物对机体的作用即药效动力学过程，药效的不同是我们对药物分类的依据，通常在我们确定所选择的药物是否适合治疗某种综合征或疾病时发挥了关键作用。机体对药物的作用即药代动力学过程，包括药物的吸收、分布和消除过程，药物的药代动力学过程对于某些特殊患者选择和使用特殊药物有着重要的实际意义，例如肾功能障碍患者。

药物的疗效取决于药物与患者体内分子的相互作用。大多数药物都是通过改变机体内特异的生物大分子的生理或生化功能而发挥作用的。受体就是其具体体现。

众所周知，由于人们在研究药物的构效关系时发现一组结构相似的药物具有相似或相反的作用，进而推断出机体内存在特异的药物受体。因此，如果一系列相关的激动剂在产生两种不同的作用时表现出相同的效应，这两种作用有可能是由相似或相同的受体分子介导的。所以，研究一系列激动剂和拮抗剂的构效关系，可以帮助我们鉴别介导某种药理学效应的受体种类。

治疗的目的应该是使药物产生满意疗效的同时尽量减少不良反应。当选择某种药物治疗患者时，临床医生必须确定最符合这一目标的用药剂量。这就需要综合药效动力学和药代动力学的规律来阐明药物的量效关系。药效动力学研究药物的浓度－效应关系，而药代动力学研究的是药物的剂量－浓度关系。药代动力学中药物的吸收、分布和消除过程决定了药物在靶器官起效的快慢和作用时间长短。药效动力学中的最大效应和敏感性等概念决定

了药物在某一浓度时的作用强弱。

了解了药物的浓度－效应关系，临床医生就能考虑到由于不同患者机体病理和生理特点的差异，患者对药物的反应会与正常人不同。

对　话

1. 师生间有关药物的对话

学生： 教授，您能给我们说说治疗的根本目的是什么吗？

教授： 治疗的根本目的是预防和治愈疾病。如果这一目的无法达到，其次的治疗目的则是使用药物缓解和减轻疾病的发展及药物对机体的破坏或致残程度。

学生： 您能告诉我们，药物的用量和疗程是如何确定的呢？

教授： 好的，药物的用量和疗程是根据所需治疗的疾病的特征决定的。例如，无并发症的尿道感染用一种磺胺药物治疗10天就可痊愈，而癫痫病大发作的病人则需用苯妥英或苯巴比妥或两药兼用终生治疗。

学生： 那么，怎样才能成功地治愈疾病呢？

教授： 成功地治愈疾病需要使用药物，药物的用量应足量以获得理想的疗效，但又不至于产生毒性反应。

学生： 各种药物的使用方法是怎样确定的呢？

教授： 过去，包括吗啡和强心苷等许多药物的治疗都是以经验观察或反复试验及失败的教训为依据的。在采用天然药物时，通常都是医生选择药物，确定剂量和给药次数，记录疗效，有毒性反应发生时再调整治疗。现在，从药物的开发到临床应用需要经过严格的审批和实验论证，以期达到最佳使用效果。

学生： 我明白了。教授，谢谢您！

教授： 不客气。

2. 药物的生物转化在何处进行?

Frank：你知道药物进入人体后，在哪里进行代谢吗?

Tony：在肝脏吧?

Frank：不完全正确。几乎机体的所有组织都能代谢药物，但肝脏是药物代谢的主要器官。其他组织如胃肠道、肺脏、皮肤以及肾脏也有较强的作用。

Tony：那什么是药物的首过效应呢?

Frank：许多药物口服后能被小肠完全吸收，然后经门脉系统首先运输到肝脏，药物在肝脏被大量代谢，这一过程称为首过效应。有些口服药物可在胃酸、消化酶或下段肠道微生物的作用下发生生物转化，且多于在肝脏代谢的数量。因此，肠道对药物的代谢也属于首过效应。

Tony：也就是说，药物口服后的首过效应可大大减少其生物利用度?

Frank：是的。所以有些药物不得不改变给药途径才能达到有效血浆浓度。

Tony：到底是什么物质导致药物在体内发生生物转化呢?

Frank：大多数的生物转化是在特殊的细胞酶催化下进行的。在亚细胞水平，这些酶位于胞膜、胞浆、核膜以及内质网、线粒体、溶酶体。

Tony：看来，药物发挥药效前已在体内经历了相当复杂的变化。

阅读材料

1. 血浆蛋白结合重要吗?

在药效动力学、药代动力学和药物相互作用中，血浆蛋白结合是一个经常提到的影响因素。然而并没有临床相关资料表明，药物的性质或药效的变化与血浆蛋白结合程度的变化有明确的关系。也就是说，药物与血浆蛋白解离能够增加游离型药物的浓

度、增强药效或许有可能产生毒性的说法似乎简单明了。但这种简单的理论只适合体外试验，而在体内这种能够消除游离型药物的开放系统中却不适用。

首先，游离型药物的数量即使发生了从1%增加到10%这种看起来很明显的变化，而实际释放到游离池的药物不会超过体内总药量的5%，这是因为即使结合率非常高的药物（例如华法林）也只有不到总量1/3的药物能与血浆蛋白结合。当然药物与血浆蛋白解离后会均匀分布，所以体内游离型药物增加5%最多只能使药物作用部位具有药理活性的游离型药物增加5%。

其次，随着血浆中游离型药物数量的增加，药物的清除率也会随之增加（如果游离型药物的清除率不变），经过4个半衰期后，游离型药物的浓度将恢复到原来的稳定水平。

血浆蛋白结合的临床重要性仅仅在于能够帮助我们检测药物浓度，当血浆蛋白低于正常时，总药物浓度也将降低，但游离型药物浓度不受影响。

2. 新药的发现

在过去的60年中，新药的发展带来了医学实践的革命，使许多过去致命的疾病几乎都可通过常规方法进行治疗，原因之一是由于开发和检验新药方法的改进。由于新技术的出现、财力的倾斜和政府对医学研究的支持使这一过程大大加速。如今，许多国家已通过立法和政府部门严密监控来规范药品检验。

开发新药的第一步是寻找或合成有前景的新药分子。根据法律，在新药投入市场之前，必须确定药物的安全性和有效性。除了进行体外研究之外，在进行人体药物试验之前还要进行动物试验，以确定药物分子的多种生物效应。人体药物试验必须包括三期，完成后才可以批准推广使用。批准推广使用后还要进行第四期试验以收集数据。

一种新药的成功开发需要大约1亿到5亿美元以上的巨大投

资。这些投资包括寻找有效新分子的劳务投资（每获得一个成功的新药大概需要合成 5000 ~ 10000 个新分子），即每一个新分子进行详细的基础和临床研究的投资及从中筛选出最终分子的投资。正是由于大多数新药的研制需要大量的投资并冒很大的风险，所以现在新药的开发大多是在制药企业的实验室中进行。但同时新药成功开发的回报也是同样巨大的。据估算，1991 年全世界处方药销售额是 2840 亿美元。另外，估计在 20 世纪后 50 年，仅在肺结核、小儿麻痹症、冠心病和脑血管疾病的治疗中，制药企业生产的药物就挽救了 150 多万人的生命，并节省了 1400 亿美元的开支。

大部分候选新药是通过下列 4 种方法中的一种或几种确定的：（1）通过化学方法修饰已知分子；（2）搜寻大量自然产物、过去发现的化学药品、或者多肽、核酸及其他有机分子；（3）在已知生物机制和化学结构基础上进行合理的药物设计及改进；（4）使用生物工程和基因克隆技术合成大分子多肽和蛋白。除了这些方法之外，现在人们更多关注的是发现全新的药物治疗靶点，例如针对第二信使的细胞内受体。

3. 重组组织型纤维蛋白溶酶原激活剂（rt - PA）的发现和开发

心血管血栓性疾病是引起死亡和残障的主要原因之一，但使用药物溶解血凝块是最近二十年才用于临床的治疗方法。在二十世纪八十年代早期，用于临床的溶栓药物仅有天然溶栓药 - 链激酶（来源于链球菌产生的一种蛋白质）和尿激酶（来源于培养的人肾脏细胞）。但由于这些药物的溶栓效应不确定，对参与凝血的关键蛋白有广泛作用，以及对血凝块和纤维蛋白缺乏选择性，以致有引起出血的危险，从而使这类药物的应用仅限制在一些学术科研机构。另外，链激酶极具有抗原性危险，有时可引起过敏反应，因此，作用更强、选择性更高的溶栓药有着巨大的临床应用前景。rt - PA 是当前溶栓治疗的核心，其研究、开发和

市场化是应用生物工程方法发现新药的一个典型范例。

1980 年，一位对血凝块研究感兴趣的比利时医师兼科学家 Desire Collen，开始使用一种人细胞系作为鲜有研究的可自然产生选择性纤维蛋白溶解物的来源，这种物质在人体内仅能痕量检测。虽然这一发现引起人们很大的兴趣，但是尚无法自然产生足量有效的这种大分子物质以供研究和使用。当时加利福尼亚生物工程公司 Genentech 新聘的一位分子生物学家 Diane Pennica 在一次学术会议上听到了 Collen 报告的初步研究结果。Pennica 也刚刚接触这一领域，并且刚开始使用生物工程方法生产另一种天然的血凝块溶解蛋白尿激酶。这两位科学家在讨论他们如何合作时，一个新的想法诞生了，从而使第一个溶栓药物成功产生，确立了血栓溶解的应用价值，跨越性开创了生物工程学产业。

Collen 当时正在寻找更为有效、安全并能人工合成的溶栓药。所以设想 t - PA——一种人自身合成的内源性溶栓物质对血凝块中纤维蛋白的亲和力应该较对循环中纤维蛋白原的亲和力高。它能在局部将纤溶酶原转变为有活性的纤溶酶，在血栓形成时应能选择性的将已形成的血凝快中不溶性的纤维蛋白水解成可溶性。同时，对其他凝血相关蛋白作用较小，因而不良反应较小，尤其是出血的危险降低。

Pennica 和他的基因工程小组相信，一旦他们找到了 t - PA 的化学序列及其人类基因的可靠来源，他们就能够克隆这一基因并能将之转导到微生物或动物细胞系，进而生产出大量的 rt - PA。当时尚无人能成功克隆并表达出象 t - PA 这样巨大和复杂的蛋白。

Pennica 及其同事花费了两年时间终于完成了遗传密码的破译、基因的转染和表达以及初期体外试验研究。而已是 Genentech 公司顾问的 Collen 同时也在两名患者身上首次证明了来源于 Bowes 细胞系的 t - PA 具有的临床溶栓效应。

临床试验和对重组物质的常规批准用了 5 年多的时间。1987

年11月，rt－PA获得了NDA的批准，并在大量的临床试验中被认可和扩展应用。rt－PA从想法的产生到药物获得批准共花费了7年时间，这是有史以来发现和开发新药耗时最少的一次。

（朱忠宁）

Unit Twelve

Text

Medical Psychology

Medical psychology is a branch of psychology and medicine. It is concerned with research in the etiology, clinical syndromes, treatment and prevention of mental disorder. The idea that medicine and psychology are somehow connected has a long history, dating back at least to ancient Greece. It became somewhat more formalized early in the twentieth century in the work of Sigmund Freud, who was trained as a physician. He noticed that some patients showed symptoms of physical illness (including paralysis, deafness, blindness, and the loss of sensation in part of the body, such as the hand) without any organic disorder. Consistent with his psychoanalytic theory, Freud believed that these symptoms were "converted" from unconscious emotional conflicts. He called this condition conversion hysteria. The need to understand conditions such as conversion hysteria led some researchers in the 1930s to study the interplay between emotional life and bodily processes. The field was called psychosomatic medicine.

Later, the society's first 25 years or so, research in psychosomatic medicine focused on psychoanalytic interpretations for a specific

set of health problems, including ulcers, high blood pressure, asthma, migraine headaches, and rheumatoid arthritis. During the 1960s, psychosomatic medicine began to focus on new approaches and theories. It is currently a broader field, concerned with the interrelationships between psychological and social factors, biological and physiological functions, and the development and course of illness.

A new field was founded in the early 1970s to study the role of psychology in illness. This field, called behavioral medicine, initially grew out of the perspective in psychology called behaviorism, which focused on the learning of behavior through classical and operant conditioning. Behaviorism was in its heyday at this time, and conditioning methods had shown a good deal of success as therapeutic approaches in helping people modify problem behaviors, such as overeating, and emotions, such as anxiety and fear. By this time, physiological psychologists had clearly demonstrated that psychological events – particularly emotions – influence bodily functions, such as blood pressure. Also, psychologist Neal Miller and his colleagues had demonstrated that physiological functions could be modified in animals through operant condition. Researchers subsequently showed that humans often can learn to control virtually any physiological system if they are given feedback as to what the system is doing. Why were these findings important? They revealed that the link between the mind and the body is more direct and pervasive than was previously thought. Soon they led to an important therapeutic technique called biofeedback, whereby a person's physiological processes, such as blood pressure, are monitored by the person so that he or she can gain voluntary control over these processes through operant condition. Biofeedback appears to be useful in treating a variety of health problems, including high blood pressure and headaches.

A third field also emerged in the late 1970s, but this one is within the discipline of psychology. It is called health psychology. Health Psychology has four goals. Let's look at some of the ways psychologists can contribute these goals.

The first goal is promote and maintain health. Psychologists study such topic as why people do and do not smoke cigarettes, use safety belts in cars, drink alcohol, and eat particular diets. As a result, health psychologists can help education programs and media campaigns to encourage healthful lifestyles and healthful behavior.

The second goal involves the prevention and treatment of illness. Psychological principles have been applied effectively in preventing illness, such as in reducing high blood pressure and therefore, the risk of heart disease and stroke. For those people who become seriously ill, psychologists with clinical training can help them adjust to their current condition, rehabilitation program, and future prospects.

The third goal focuses on the causes and detection of illness. Psychologists study the cause of disease; the studies we saw earlier showing the importance of personality factors in the development of illness are examples of this work. Psychologists also study physiological and perceptual processes. This knowledge has been applied to the diagnosis of problems in people's vision and hearing, for example.

The last goal is to improve the health care system and health policy. Psychologists contribute toward this goal by studying how patients are affected by characteristics or functions of hospitals, nursing homes, medical personnel, and medical costs. With the resulting knowledge, they can make recommendations for improvement, suggesting ways to help physicians and nurses become more sensitive and responsive to the needs of patients and to make the system more accessible to individuals who fail to seek treatment.

The goals of the three fields are very similar, and the overlap in the knowledge used in these fields is extensive. Perhaps the main distinction between them is the degree to which they are interdisciplinary. Behavioral medicine has the most diverse membership, drawing knowledge directly from a wide variety of disciplines in their research. Psychosomatic medicine continues to be closely allied with medical disciplines, especially psychiatry. And health psychology is a subfield of psychology. As a result, health psychologists are able to draw directly on the many other subfields within the discipline: clinical, developmental, experimental, physiological, and social psychology.

It is important to realize also that these three fields are separate *mainly in an organizational sense*. Although they have slightly different perspectives, all three fields share the view that health and illness result from the interplay of biological, psychological, and social forces. As this suggests, all three fields are interested in knowledge from a wide variety of disciplines and are engaged in a cooperative effort to enhance wellness and reduce illness.

New Words

psychology [sai'kɔlədʒi] *n.* 心理；心理学
paralysis [pə'rælisis] n. 瘫痪，麻痹
psychoanalytic ['saikəu,ænə'litik] adj. 心理分析的
hysteria [his'tiəriə] n. 癔症，歇斯底里
psychosomatic [,saikəusəu'mætik] n. 由心理压力引起的，心身性的，心身医学的
asthma ['æsmə] n. 气喘，气喘病，哮喘
migraine ['mi:grein;'maigren] n. 偏头痛
behaviorism [bi'heiviəriz (ə) m] *n.* 行为主义学派，行为主义者
heyday ['heidei] n. 全盛时期

overeating ['əuvə'i:tiŋ] n. 贪食，贪食症
pervasive [pə:'veisiv] adj. 蔓延的，遍布的，弥漫的，渗透的
rehabilitation ['ri: (h) ə,bili'teiʃən] n. 修复，恢复（原有地位或正常生活），复原
interdisciplinary [,intə (:)'disiplinəri] adj. 各学科间的，科际的，跨越学科的
psychiatry [sai'kaiətri] n. 精神病学，精神病治疗法

Phrases and Expressions

clinical syndromes　临床综合征
mental disorder　心理障碍，精神疾病，心理疾病
organic disorder　器质性病变
rheumatoid arthritis　风湿性关节炎
behavioral medicine　行为医学
classical and operant conditioning　经典性和操作性条件反射
voluntary control　自主控制
health psychology　健康心理学
healthful lifestyles　健康生活方式
healthful behavior　健康行为
nursing homes　疗养院

Questions

1. What is the professional relationship between psychology and clinical disorders?
2. Please say something about Sigmund Freud.
3. How about behavioral medicine and health psychology?
4. What are the goals of health psychology?
5. Please tell something about the healthful lifestyles and behavior as possibly as you can.

6. Make a speech or write a summary about the text.

Dialogue

Mental Consult

Psychologist : What's wrong with you?

Wife : I heard a friend of mine talk about you and my ears perked up, because I thought about my husband's problems. He was most active until about fourteen years ago, when he had a doubt with depression. He was treated by a local psychiatrist with several antidepressants, but never responded. He finally got better without medication.

Psychologist : How do you feel now?

Mr. Brink : Well…I don't know…Bad, I feel bad. I put everything off, don't want to do anything. See… I can't even speak up. She does all the talking.

Wife : And it was just the opposite before he got sick, It was me who always was nervous.

Psychologist: What do you feel when you feel bad?

Mr. Brink : I worried. I worried about coming here. I worried all day and night.

Psychologist : You worried in the night. Is that different from the morning?

Mr. Brink : In the morning I'm numb. I don't want to get up. I don't want to do anything. I don't want to talk.

Psychologist : What feel worse, the morning or evening?

Mr. Brink : I'd have to say the morning …like now.

Psychologist : Is there anything that will make you feel better for a

while?

Mr. Brink : No, nothing, nothing at all.

Wife : Yesterday he was feeling well. His son was over and took him out. And he always enjoys that a lot.

Psychologist : Having your son over makes you feel better?

Mr. Brink : (His face seemed to drop, the lines in his face deepened, he looked ashen.) Maybe for a while (with a *doubted and weak voice*).

Psychologist : Talking about your son cheers you up?

Mr. Brink : Not really. Nothing makes a real difference. Talking usually makes me feel worse.

Psychologist : When I talk to you, you don't seem that depressed

Mr. Brink : For a short while I can put up a front, but I feel worse behind it.

Wife : He had to do that in his business.

Mr. Brink : I can't accomplish anything. I can't do my work. I just sit there. I don't know what to do first.

Psychologist : How does the future look to you?

Mr. Brink : I will never get better.

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Reading Material

1. Study of the Implicit of Mental Health and Need of Mental Health Service for Different Social Classes

A questionnaire was used to investigate the implicit concept of mental health of different social classes and the needs of mental health

service. The results indicated that: (1) There were significant differences of the implicit concept of mental health between people from different social classes and with different ages. No significant difference was found between male and female. (2) The most important positive components of the implicit concept of mental health were "optimism, ardor, pure - heartedness" and "quiet in mind and peace in disposition, be happy to render helps to other", While the negative ones were "unsociable, uncommunicative and eccentric disposition" and "pessimism, despair of life". (3) The most urgent task for psychologists was "to propagandize knowledge of mental health, offering service of mental health.", for few people could confront to their own mental needs, and only 3.9% subjects are willing to accept psychological service and consultation.

2. Research on Health and Lifestyle

In 1965, Nedra Belloc and Lester Beslow began a project to study the importance of personal lifestyles on people's health. The researchers surveyed nearly 7, 000 adults who ranged in age from about 20 to over 75, and asked them two sets questions. One set asked about the health of these people over the past 12months - - - for instance, whether illness had prevented them from working for a long time, forced them to cut down on other activities, impaired their continued activities, and reduced their energy level. The second set of questions asked about their health practices regarding seven issues: sleeping, eating breakfast, eating between meals, maintaining an appropriate weight, smoking cigarettes, drinking alcohol, and getting physical activity.

Were these lifestyles factors important? The survey revealed that

the physical health of these people was strongly related to the following health practices: (1) Sleeping seven to eight hours a day. (2) Eating breakfast almost every day. (3) Never or only occasionally eating between meals. (4) Being at or near the appropriate weight for their height. (5) Never smoking cigarettes. (6) Never or moderately drinking alcohol. (7) Regularly getting physical activity.

When the researchers compared the data for subjects in different age groups, they found that at each age health was typically better as the number of healthful practices increased. The impact of these health practices is suggested by the finding that the health of those who "reported following all seven good health practices was consistently about the same as those 30 years younger who followed few or none of these practices".

Were these health practices important in the future health of these people? Berslow has described later studies of the same group of subjects. One study determined which people had died in the nine and a half years after the original survey. These data were then separated according to the age, sex, and number of healthful behaviors the people reported practicing in the original survey. The important finding was that the percentage dying generally decreased with increased in the number of healthful behaviors practiced, and this impact was greater for older men than for younger ones. The results for the female subjects were similar, but the impact of these health practices was not as strong.

"Why don't people do what's good for them?" We have all heard that question before. There's no simple answer – there are many reasons. One reason is that less – healthful behaviors often bring immediate pleasure, as when the person has a "good tasting" cigarette or ice cream. Long – rang negative consequences seem remote, both in time

and in likelihood. Another reason is that people sometimes feel social pressures to engage in unhealthful behavior, as when an adolescent begins to use alcohol or drugs. Also, some behaviors can become very strong habits – perhaps involving a physical addiction or psychological dependency, as happens with drugs and cigarettes – and quitting is very difficult. Lastly, sometimes people are simply not aware of the danger or how to change their behavior. As psychologist Carl Thoresen has pointed out, "people need to be taught how to be more caring and more responsible for their own health and well – being, especially when the social environment commonly promotes irresponsible behavior."

Do you believe, as many do, that people with ulcers tend to be worriers or "workaholics"? or that people who suffer from migraine headaches are highly anxious? If you do, then you believe there is a link between personality and illness. Is this belief correct?

Researchers have found evidence for the view that personality plays a causal role in illness. For instance, people whose personalities include high levels of anxiety, depression, and anger/hostility seem to be "disease – prone" for developing a variety of illness, particularly heart disease. The three emotions involved in the disease – prone personality are reactions that often occur when they have more work to do than they think they can finish or when a tragedy happens.

People differ in the way they deal with stressful situations. Many people approach these situations with relatively positive emotions. Their outlook is more optimistic than pessimistic, more hopeful than desperate. These people are not only less likely to become ill than are people with disease – prone personalities, but when they do, they tend to recover more quickly. A dramatic well – known anecdotal example of the role of this optimistic and hopeful outlook is the case of Norman Cousins, the former editor of Saturday Review, who devel-

oped an "*incurable*" and usually fatal illness. His reaction to the prognosis was unusual: he decided he should not believe his doctors' pronouncement on his medical treatment, but with high doses of vitamin C and lots of laughter, which he got by watching comic films like those of Groucho Marx and Laurel an Hardy. As his condition began to improve, he came to believe he was recovering because his optimism enabled him to mobilize his body's resources fight the disease.

The link between personality and illness is not a one – way street: illness can affect one's personality, too. People who suffer from illness and disability often experience feelings of anxiety, depression, anger, and hopelessness. But as psychologists Irwin and Barbara Sarason have pointed out: A physical illness does not necessarily have to be catastrophic to exert a psychological impact. Anyone who has had the flu, has a sprained ankle, or has had a toothache knows how much psychological damage these relatively minor problems can cause. Of course, the more serious the physical disorder was, the greater the likelihood that it will significantly affect a person's thoughts and feelings. These psychological changes compound the detrimental effects of the person's physical condition. People who are ill need to overcome their negative thoughts and feelings in order to speed their recovery.

参考译文

课　文

医学心理学

医学心理学是心理学和医学的分支，它主要研究心理疾病的病因学、临床表现、治疗和预防。心理学和医学相结合已有很长

的一段历史，至少可以追溯到古希腊。早在 20 世纪，弗洛伊德作为一名内科医生就已经开始把二者结合起来进行研究。在研究中他注意到，一些病人有身体疾病方面的症状（包括瘫痪、耳聋、失明和身体某一部分例如手失去感觉），但没有任何器质性病变。按照他的心理分析理论，弗洛伊德认为这些症状是由无意识的情感冲突转换而来的，他把它命名为癔症型转换。为了掌握诸如癔症型转换等情况，一些研究者在 20 世纪 30 年代就开始研究情绪和身体之间的相互关系，这个领域被称为心身医学。

之后，在这一领域形成的最初 25 年左右，心身医学方面的研究主要集中在对一系列特殊的健康问题的心理分析，包括溃疡、高血压、哮喘、偏头痛和风湿性关节炎。20 世纪 60 年代，心身医学开始关注新的方法和理论，目前已成为一个非常广阔的领域，它主要研究心理因素和社会因素之间、生物功能和生理功能之间、疾病的发生与发展之间的关系。

20 世纪 70 年代，一个新的领域出现了，它主要研究心理因素在疾病中的作用，这个领域被称为行为医学。该领域起源于心理学中的行为主义学派，行为主义学派主要研究通过经典性和操作性的条件反射而产生的行为。行为主义学派当时正处于鼎盛时期，并且条件反射作为治疗手段在帮助人们矫正问题行为时已经取得了很多成功，例如贪食症、焦虑和恐惧等情绪行为。这时，生理心理学家已经明确了心理事件特别是情绪问题会影响身体功能，例如血压。心理学家米勒和他的同事们也发现，操作性条件反射可以矫正动物的生理功能。研究人员随后又发现，如果给人类生理反馈，人类通常确实能够学会控制自己的任何生理系统。这些发现为什么如此重要呢？因为这些现象表明，心理和身体方面的联系比以往认为的要直接且广泛得多。不久，他们就发展了一个被称为生物反馈疗法的重要治疗技术，该疗法可以通过操作性条件反射使人能够自主控制自身的生理过程例如血压的变化，它在治疗高血压和偏头疼等各种疾病时非常有效。

第三个领域也是在二十世纪七十年代出现的，但这个领域是心理学的一个分支学科，被称为健康心理学。健康心理有四个目标，让我们来看看心理学家提供的可达到此目标的一些方法。

第一个目标是促进和维护健康。心理学家研究这样的课题，例如人们为什么有或者没有吸烟、开车系安全带、饮酒和特殊饮食的习惯。通过研究，健康心理学家能帮助教育节目和媒体活动去鼓励人们采纳健康的生活方式和行为。

第二个目标是预防和治疗疾病。心理学原则已在预防疾病方面得到了有效的应用，例如降低血压后，可降低心脏病和中风的发病风险。对较重的病人，受过临床训练的心理学家能够帮助他们调整自身以适应目前的状况，制订康复计划和未来的设想。

第三个目标是研究疾病的病因和诊断。心理学家研究疾病的病因，例如我们先前提到的性格因素在疾病发展中重要作用的研究，还进行生理过程和认知过程的研究。这些成果已经应用于视觉和听觉疾病的诊断。

最后一个目标是改进医疗体系和卫生政策。心理学家通过研究医院、疗养院、医护人员和医疗消费的特征及功能对病人产生怎样的影响来实现这个目标。通过研究，他们可以提出改善的意见，和使医生和护士增强对病人需求的敏感和责任，以及建立急需治疗的个体更易于接受的医疗体系的建议。

这三个领域的目标是非常相似的，领域内的知识交叉也是很广泛的。或许各交叉学科之间的主要区别只是程度的问题。行为医学的分支学科种类最多，该研究领域的知识直接来源于众多学科。心身医学与医学学科的紧密联系次之，特别是精神病学。健康心理学是心理学的一个分支，因此，健康心理学家能够直接接近临床心理学、发展心理学、实验心理学、生理心理学和社会心理学等许多其他的心理学科领域。

认识到这三个领域之间主要是组织意义上的差异是非常重要的，尽管它们之间有所差异，但这三个领域有一个共同的观点，

那就是健康和疾病都是生物、心理和社会因素相互作用的结果。因此，这三个领域都对很多其他学科的知识感兴趣，并为努力促进人类健康和减少疾病而携手合作。

对　话

心理咨询

心理学家：请问您为什么来看病？

妻子：因为我丈夫的问题，所以当我从朋友那儿听说你的时候就引起了我的注意。十四年前他还是一个非常活跃的人，后来有点消沉，经精神病医生的几种抗抑郁药治疗后，没有什么效果。后来不吃药倒渐渐好起来了。

心理学家：您现在感觉如何？

Brink 先生：噢……我不知道……不好，感觉很糟糕。我无论做什么事，总是拖拖拉拉，并且不想做任何事，甚至不能说话。我妻子替我都说了。

妻子：在他生病之前正好相反，我总是感觉很紧张。

心理学家：当您觉得不好的时候有什么感觉？

Brink 先生：我担心，我担心来这里，我每天从早到晚担心。

心理学家：您在晚上担心，和早上有什么不同吗？

Brink 先生：我在早上很麻木，我不想起床，不想做任何事，不想说话。

心理学家：是早上还是晚上感觉更不好？

Brink 先生：我觉得是早上，就像现在。

心理学家：有什么事能让您暂时觉得好一些吗？

Brink 先生：没有，什么事也没有。

妻子：昨天他感觉好一些，他儿子过来带他出去了。他多少还是喜欢出去。

心理学家：您儿子过来看您可以让您感觉好些，是吗？

Brink 先生：（脸低了下去，脸上的皱纹更深了，看上去脸色发灰。）可能会好一会儿（声音犹豫而低弱）。

心理学家：谈到您儿子可以使您高兴一些吗？

Brink 先生：也不是，都没什么不同，谈话通常使我感觉更糟糕。

心理学家：当我和您谈话时，您好像并不抑郁。

Brink 先生：有一小会儿，我外表看上去并不抑郁，但我内心感觉还是很糟糕。

妻子：在生意上他不得不这样做。

Brink 先生：我不能完成任何事情，我只是坐在那却不能工作。我不知道先干什么。

心理学家：您感觉前途如何？

Brink 先生：不会更好。

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阅读材料

1. 不同社会阶层心理健康观念及心理健康服务需求状况的调查

应用问卷调查，对不同社会阶层的心理健康观念及心理健康服务需求状况进行了调查研究。结果表明：（1）不同社会阶层、不同年龄人群的心理健康观念显著不同，但男性和女性之间没有发现显著性差异。（2）心理健康的人应具有的最典型特征是“处事乐观、热情、诚恳”和“心平气和、淡泊名利、乐于助人”。心理不健康的人所表现得最典型特征是“性格孤僻、与人不合群”和“悲观、对生活失去信心”。（3）对心理学家来说，最紧迫的任务是“宣传心理健康知识、开展心理卫生服务”，因为目前极少有人能够正视自己的心理健康需求，仅 3.9% 的人愿意接受心理健康服务和咨询。

2. 关于健康和生活方式的研究

1965 年，Nedra Belloc 和 Lester Beslow 开始了一项关于个人生活方式对健康影响重要性的研究计划。研究人员用两套问卷调查了大约 7000 个年龄从 20 岁到 75 岁的成年人。一套问卷调查这些人过去 12 个月的健康情况，例如是不是疾病迫使其离开工作岗位很长一段时间，迫使他们减少一些其他的活动，削弱他们继续活动的能力，降低他们的能量水平。第二套问卷调查了关于他们健康活动的七个方面：睡眠、早餐、加餐、控制体重、吸烟、饮酒和体育锻炼。

这些生活方式因素对健康是不是很重要？调查显示，这些人的身体健康和下面这些健康习惯之间有很大的关系：（1）每天睡 7 到 8 个小时。（2）几乎每天吃早饭。（3）从不或偶尔加餐。（4）体重与身高相符或基本相符。（5）从不吸烟。（6）从不或适度饮酒。（7）有规律的体育锻炼。

当研究人员比较不同年龄组受试者的资料时发现：无论在哪一个年龄组，健康习惯越多，身体越健康。结果表明，这些健康习惯对身体的影响表现为，那些能坚持上述七个方面健康习惯的人，与较其年轻 30 岁但很少或没有这些健康习惯者的身体健康状况相似。

这些健康习惯对未来的健康重要吗？Berslow 对同一组受试者进行了深入的研究，观察 9 年半后受试者的死亡情况，然后将数据按照年龄、性别、调查最初时的健康习惯进行分类。发现随着受试者健康习惯数量的增多，死亡百分率减少，而这种情况对老年人的影响大于对年轻人的影响，对女性的影响基本相似，影响程度不是很大。

“为什么人们不做些对自己健康有利的事呢?”以前我们总是听到这样的问题。关于这个问题没有一个简单的答案，有很多原因。一个原因就是无益于健康的行为往往给人们带来短暂的快乐，例如当人们偷尝香烟或冰激凌时，长期的负面结果无论是在

时间上还是在可能性上都是很遥远的。另一个原因就是当人们有时感到社会压力时就会产生不健康的行为，例如当一个青少年开始喝酒和吸毒时。当然，一些行为可能变成十分顽固的习惯，可能还产生了身心依赖，例如吸毒和吸烟就很难戒掉。最后一个原因就是有时人们对危险没有警惕或是不知道该如何改变他们的行为。正如心理学家 Carl Thoresen 指出的：应该教会人们如何对其健康和幸福予以更多的关心和责任，特别是当社会环境普遍促进不负责任行为的产生时。

正如许多人那样，你是否相信溃疡病患者往往是忧虑的人或工作狂，而偏头痛的人常常很焦虑？如果你相信，那么在性格和疾病之间可能存在着一定的联系，这种观点正确吗？

研究人员已发现了支持性格在疾病中扮演着重要角色的证据。例如，那些个性中包含高度焦虑、抑郁、愤怒/敌视的人具有患病倾向，易患各种疾病，特别是心脏病。当人们有许多比他想象中更多的未完成工作或悲剧发生时，这三种有患病倾向的性格情绪容易导致人发病。

人们处理压力的方式不同。许多人用相对正面的情绪处理，对前景的看法乐观多于悲观、希望大于失望，与有患病倾向性格的人相比，他们不容易得病，即使得了病也能很快恢复。一个众所周知的关于乐观情绪和满怀希望对健康产生影响的戏剧性趣闻是 Norman Cousins，他是原《星期六评论》的编辑，得了一种不可治愈的、一般认为是致命的疾病。但他对该病预后的反应不同寻常：他下决心不相信医生给他的药物治疗，而采用大剂量维生素 C 和经常看 Groucho Marx 、Laurel 和 Hardy 的喜剧电影而大笑的方法来治疗疾病。当身体状况开始好转时，他开始相信他之所以恢复是因为他乐观的情绪调动了身体内部的力量来战胜疾病。

性格和疾病之间的联系不是一条单行道，疾病也会对一个人的性格产生影响。长期受疾病和残疾折磨的人经常感觉到焦虑、抑郁、愤怒和绝望。但是，正如心理学家 Irwin 和 Barbara Sara-

son 所指出的：身体上的疾病不一定总是灾难性地产生心理影响。任何患过感冒、扭伤脚踝或者牙痛的人多会知道这些小毛病带来的心理伤害到底有多大。当然，身体上的疾病越严重，影响一个人的思想和情绪的可能性就越大。这些心理变化加重身体状况的损害。因此，那些患病的人需要克服负面的想法和情绪以尽快恢复身体健康。

（李俊丽　李　铮）

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