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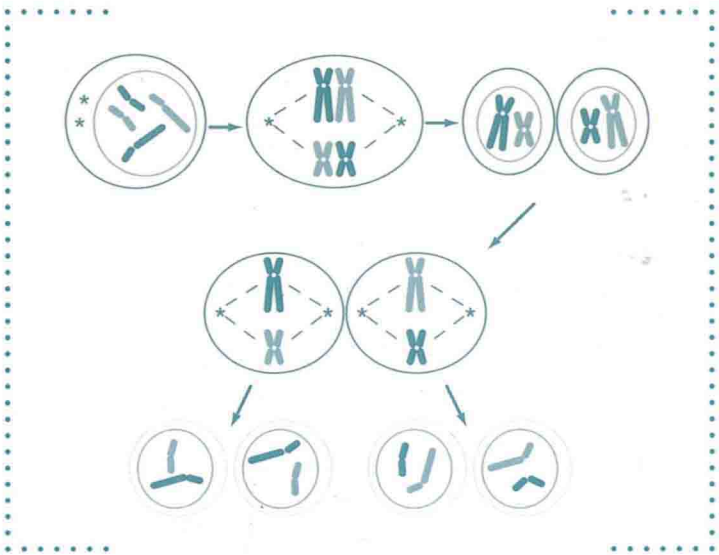
BASIC CONCEPTS IN Medical Genetics

A STUDENT'S SURVIVAL GUIDE

Marshall Horwitz



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BASIC CONCEPTS IN Medical Genetics

A STUDENT'S SURVIVAL GUIDE

Marshall Horwitz

Do you find medical genetics intimidating?

If so, you can relax. This great time-saving guide offers all the help you need to master the complete medical genetics course. Compact yet comprehensive,

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BASIC CONCEPTS IN Medical Genetics

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医学遗传学基本要点

BASIC CONCEPTS IN Medical Genetics

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Notice

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影印出版说明

“医学生复习指南丛书”是美国医学生所用的基础医学阅读参考书系列之一，也是参加“美国医生执照考试”（United States Medical Licensing Examination，USMLE）考前复习的主要参考书。由《生理学基本要点》、《生物化学基本要点》、《免疫学基本要点》、《药理学基本要点》、《病理学基本要点》、《医学遗传学基本要点》、《细胞生物学与组织学基本要点》、《胚胎学基本要点》、《神经科学基本要点》等组成。

本丛书内容主要为基础医学各核心课程中的基本概念及重点内容，涵盖了“美国医生执照考试”（USMLE）的主要考点内容，并用容易理解与掌握的方式对各个学科的难点内容进行了讲解。在编写方式上，作者用简明易懂的文字和大量的图表进行解释，便于学生掌握学科的重点内容，可使学生用最少的时间对学科的内容有一个完整的概念与基本了解。在取材上经过作者的精心取舍，注重知识的系统性和相关知识的联系，加强了临床应用必需的内容，因而在内容的深度和广度上比较适合医学本科教育的需要，也符合医学基础服务于临床的宗旨。例如：“细胞生物学与组织学基础教程”中不仅讲述了从细胞膜至细胞核的基本知识，还介绍了各种组织和各个器官的结构和功能；“医学遗传学基础教程”从遗传学的基础概念联系到大量的临床遗传性疾病；“胚胎学基础教程”讲述了许多先天性畸形的发生机制和危险因子……这样的编排不仅使医学基础知识紧扣临床实际，还会增强学生运用知识的能力。当然，在相互联系中更能巩固所学知识的记忆。

本丛书写作文字流畅，可读性强；条理清晰，方便查阅。对于中国的医学生来说，使用本丛书不仅能使他们掌握各学科的专业基础知识和基本概念，同时，在学习过程中，还能学到更加地道的英语表达方式，提高其专业外语水平。本丛书可作为医学基础课双语教学的英语教学参考书，也是参加美国“医生执照考试”（USMLE）的中国医学生和医生考前复习的必备参考书。

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CHAPTER 1

INTRODUCTION

Sometime early in the twenty-first century—probably before you finish medical school—the human genome will be sequenced in its entirety. The three billion basepairs of the haploid human genome represent about the same amount of data as encoded in just a single CD-ROM. It is indeed mind boggling to consider the fact that so little software can encode the designs for such a complicated machine, chiefly, a human being.

But rather than reducing humanity to such a statistic, we prefer to turn the fact on its head and note that humans accomplish at least one feat that no computer will for quite some time: we can take a CD-ROM worth of information and squeeze it into the confines of a tiny cell with volume that is less than what a CD takes to store just a single bit of information. Given that there are about a trillion cells in a human being, each containing a complete copy of the human genome in itself, our bodies enshrine and manage unfathomable volumes of data. Yet a change in as little as just a single bit (one basepair), if one is unlucky, can give rise to cancer or a new mutation responsible for an inherited disease. The fact that this process works so well, for most of us, most of the time, is testimony to just how remarkably elegant the human machine is.

But, of course, things do go wrong sometimes. The DNA mutates, the information is lost or scrambled, and the result is a genetic disease, whose legacy may be continued inheritance in a family's lineage for untold future generations, or, of even more immediate concern to that person, a life-ending malignancy. Understanding human heredity and how it relates to disease is the goal of this text.

Current statistics offer a compelling argument for the role of a course in genetics in contemporary medical education. Genetics issues are present at every stage of life.

About 50% of all first trimester spontaneous abortions result from a chromosomal abnormality. About 3% of all newborns have a major genetic disease. About a third of all pediatric hospital admissions are the result of

genetic disease. About half of all pediatric deaths are ultimately attributable to genetic disease. About 2% of all adults will suffer from a single gene genetic disease. The vast majority of common diseases like diabetes mellitus, atherosclerotic vascular disease, and mental illness are the result of the additive effects of genes conferring variable degrees of risk interacting with the environment.

Times are changing fast enough that a working knowledge of the basics of human genetics are most likely to factor even more prominently in any physician's career from our present time onward.

We might like to entitle this book *Human Genetics for Dummies*. We cannot because the publisher of that popular line of books would not allow it. But, we also should not. That is because this material is sufficiently complicated and fast-changing enough that it is a difficult topic for anyone to comprehend. Indeed, one recent study found that physicians in practice incorrectly ordered a genetic test predicting colon cancer about one-half of the time and misinterpreted the results of that test about a third of the time. For a test designed to give a discrete answer, this sort of incompetence renders such a powerful test virtually meaningless or, even worse, downright dangerously misleading. Imagine the consequences of falsely reassuring someone that they are not likely to inherit cancer, or, of mistakenly leading an individual to believe that they will inherit cancer. Such false counsel can have profound influences on the decisions one will make in life: if one will marry and have children, whether one will continue to seek employment, or even if one will choose to end his or her life. As genetic tests become more ubiquitous and more complicated, the potential for misinterpretation of tests becomes even greater. There is also the problem of misapplication of correctly interpreted tests; as a society, we have yet to come to grips with the consequences of such testing. It is, therefore, an imperative that the modern physician become fully versed in this stuff.

This book is intended to be a reasonably complete synthesis of fundamental genetic principles illustrated with clinical examples, and one that can be read in a single, long sitting. It is an outgrowth of the syllabus used to teach medical genetics to second year medical students at the University of Washington, in a 22-hour course comprised of lecture and small group problem-based learning.

This text benefits from the contributions that numerous faculty members and fellows have made to the course over the years. We gratefully acknowledge these individuals, many of whom were our own teachers: Arno Motulsky, George Stamatoyannopoulos, Roberta Pagon, Wylie Burke, Peter Byers, Ron Scott, James Evans, Thomas Bird, Virginia Sybert, Louanne Hudgins, Edith Cheng, Kathy Leppig, Robin Bennett, Michael Raff, Hanlee Ji, Mark Hannibal, Melissa