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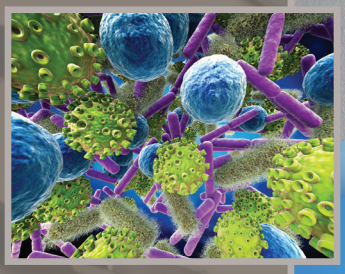
Essentials of Clinical Infectious Diseases

Second Edition



William F. Wright

Essentials of Clinical Infectious Diseases

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Second Edition

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To Susan—my beautiful wife, best friend, and the wind beneath my wings. I am the luckiest man in the world to be married to a magnificent and brilliant woman like you. Sharing our life and love along this journey together is a blessing beyond words. I am grateful for your unwavering love, faith, and support. This book is affectionately dedicated to you, without whom this second edition would not have been completed.

CONTENTS

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PREFACE

We have been gratified by the popularity of the first edition of *The Essentials of Clinical Infectious Diseases*. It has been more than five years since the first edition of this book presented readers with the essential aspects of the subspecialty infectious diseases. The popular reception of the book and the rapid expansion of medical knowledge call for a new edition to assist readers through this medical transformation—*from a demystified wonder to a commonplace tool in medical education*.

This edition (a) provides technical corrections, updates, and clarifications in all 45 chapters of the original book; (b) adds six new chapter topics; (c) includes new developments that are consistent with the published peer-reviewed medical literature, published relevant clinical practice guidelines, and updated bibliographical references at the end of each chapter; and (d) elucidates subtle issues that readers and reviewers have found perplexing, objectionable, or in need of elaboration.

Our main audience remains the students and medical providers in training. However, information within this book evolved from prior formal didactic lectures or bedside clinical teaching on clinical infectious diseases, microbiology, and antimicrobial pharmacology that was delivered to help students, residents, fellows, and primary care physicians. Current basic science and clinical concepts regarding each relevant infectious disease topic are still written as a synoptic account to make these topics clear and practical for the readers of this text. Teachers who have taught from this book before should find the revised edition more lucid and palatable. We continue to adhere wherever possible to a standard pattern of description that aims to define the topic; provide an introduction that would include classification, pathophysiology, and epidemiologic information; list relevant causative microorganisms; describe the clinical aspects and approach to the topic with the physical examination and relevant laboratory methods, diagnostic imaging, and appropriate antimicrobial therapy. This updated essentials text also includes new chapters that readers will hopefully find useful beyond the basic clinical syndromes: introduction to clinical reasoning and statistics, introduction to antimicrobial stewardship, and basic approach to travel medicine.

While medicine continues to evolve and the amount of knowledge a learner must retain may seem daunting, knowing basic concepts can make the approach to a patient with a possible infection an easy and exciting task. Although this text is arranged by certain infectious disease topics, patients typically present with a constellation of symptoms and signs. Knowing basic concepts, therefore, can help clinicians arrive at the diagnosis of the disease causing the patient's symptoms and signs. This process (clinical problem solving) begins by a discussion with the patient of the chronology of events associated with the symptoms or signs experienced as well as asking appropriate relevant questions. Additionally, a complete physical examination is then performed for diagnostic clues that then lead to the formulation of the most appropriate differential diagnosis that is based on an understanding of these basic concepts. Based on the initial discussion and examination, appropriate laboratory or imaging tests are ordered to support or refute the diagnostic considerations. The goal of this text is to help guide

the reader through the diagnostic evaluation as well as the process of caring for the patient with an infection.

The editor and contributing authors have collaborated to prepare chapters consistent with the peer-reviewed published medical literature, published clinical practice guidelines and their teaching, clinical, and research activities. Each chapter concludes with important medical references that may also include reference to a "classic" article regarding the infectious disease topic that can be utilized by the reader as additional reading. Through this text the authors strive enthusiastically to impart to readers a solid fundamental knowledge and approach to clinical infectious diseases that will sustain them adequately in their chosen medical professional career.

William F. Wright, DO, MPH

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1

INTRODUCTION AND BASICS OF CLINICAL REASONING

William F. Wright

I. INTRODUCTION. Akkadian cuneiform inscriptions from the 6th century BCE suggest that medicine of early Mesopotamian societies involved supernatural interpretations of disease with blaming of gods and ghosts frequently. Medical epistemology in Hellenistic Palestine and Greco-Roman societies from the 5th century BCE embodied the philosophical notion of both a macrocosm and microcosm. The writings of Aristotle, as well as early Greek philosophers such as Plato and Pythagoras, proposed the world, or macrocosm, was composed of the four elements of air, earth, fire, and water. This corresponded to a microcosm with the harmonious balance of four bodily elements (blood, phlegm, yellow bile, and black bile), which were known as humors. In his treatise, *On the Nature of Man*, Hippocrates introduced the classic theory of humors and their imbalances as a means of explaining disease. The Roman physician Galen endorsed this pathophysiology and further defined medicine for Medieval Western Europe. The classic theory of humors predominated medical thinking until the 19th century when both Louis Pasteur and Robert Koch provided proof of the microbial basis of disease. This ushered in the era of what would now be considered a rational scientific basis of medicine.

Modern clinical medicine and infectious diseases have dramatically changed over the past century. The practice has evolved from a healing art in which standards were based mainly on the personal experience of physicians to a discipline focused on the scientific method and evidence-based practice standards. While scientific advances serve as the evolutionary basis for the diagnostic and therapeutic approaches to common medical and infectious-disease conditions, reconciling the traditional physical diagnostic approach with contemporary diagnostic methods has been a continuous process throughout the history of medicine and clinical infectious diseases. The approach to the patient with an infectious disease is still best accomplished by a systematic method that combines the critically important comprehensive history and physical examination with the added benefits of contemporary technology. This process, the basis of the fundamental skills of medical diagnosis and treatment, strives to improve the physician's clinical reasoning and includes:

1. Understanding disease definitions, mechanisms, and patterns
2. Identifying the patient's chief complaint and performing a chronologically accurate medical history
3. Formulating a differential diagnosis based on the chief complaint and medical history (also known as the pretest probability)
4. Performing physical-examination maneuvers that will support or refute the conditions being considered in the differential diagnosis

5. Ordering appropriate diagnostic and laboratory tests and interpreting the results in relation to the differential diagnosis (also known as the posttest probability)
6. Implementing an appropriate evidence-based treatment plan

The purpose of this clinical reasoning is to establish a systematic and rational approach to medical decision making that allows the physician to explain the patient's symptoms based on one unified diagnosis (i.e., Occam's razor).

Critically important when applying this process to clinical infectious diseases are the chief complaint and an extended medical history that ideally includes antibiotic uses and allergies, past medical conditions and/or infections, sexual practices, drug use, travel destinations, occupational history, screening tests (e.g., purified protein derivative [PPD]), and vaccinations, which when taken together, provide important clues to the risk of acquiring an infection. However, one of the more difficult processes in clinical infectious diseases is the synthesis of all data including organisms identified in the microbiology laboratory to distinguish between an infectious process and colonization. Colonization is generally considered to be the presence of a particular microorganism or group of microorganisms (i.e., normal flora) in which their presence does not create a specific host immune response (i.e., infection). In contrast, infection is most commonly due to the invasion of body tissues with a particular microorganism or group of microorganisms, which elicits an immune response that results in a disease state.

II. EVIDENCE-BASED MEDICINE BASICS.

A group of further categories highlighting important concepts regarding clinical reasoning and evidence-based medicine principles is listed in the following. These concepts should be kept in mind when evaluating all encountered patients, including infectious diseases, so as to provide a systematic and rational approach to the clinician's medical decision making.

A. Basics of Clinical Reasoning

1. **Differential diagnosis.** The differential diagnosis is a systematic process for considering the most likely possible causes of a patient's symptom or physical finding. This process begins with evaluating a hypothesis by matching the patient's findings with the clinician's internal understanding of disease. Most often an associative model of disease, also known as pattern recognition, is used that consists of clinical findings, illness progression, predisposing characteristics, and complications that are associated with a disease.

   Clinical hypothesis generation begins with the patient's chief complaint and a chronologic account of illness from its beginning. This approach provides valuable information and perspective on the patient's illness. It also respects the patient in allowing time to recount the story as well as provide the clinician time to think, write down some diagnoses to consider, and observe the patient for diagnostic clues. Once the patient has provided a chronologic account of the illness the clinician should ask specific questions to test each of the initial diagnostic hypotheses (e.g., cross-examination history taking). The combined patient recounted and cross-examined history (e.g., chief complaint, history of present illness, and past medical–surgical history) should generate the most hypotheses. The physical examination is then usually the time to gather objective physical clues to rank, confirm, or discard a hypothesis. Remember that a pathognomonic finding usually improves diagnostic efficiency and establishes a diagnosis for one disease, but very few of these findings exist.

When the considered hypotheses have been ranked in order of plausibility, the clinician then has to decide whether to withhold any further testing or treatment, begin treatment without further testing, or gather more information with diagnostic testing prior to beginning treatment. The choice among these three alternatives is guided by probability and utility (e.g., benefit vs. harm).

2. **Probability.** Probability in medicine is referred to as either the present state of the patient or the possibility of a future patient event. Predictors of the present state of the patient would involve information from a ***cross-sectional design study***. Predictors of a possible future event of the patient would involve information from a ***cohort design study***.

   a. **Pretesting probability.** Defined as the probability of a patient having the target disorder before a diagnostic test result is known. Mathematically, it can be calculated as the proportion of patients with the disorder divided by both those with and without the disorder expressed as a percentage.

   $$\text{Pretesting probability} = \text{Disease}/\text{Disease} + \text{No disease}$$

   b. **Posttesting probability**. Defined as the probability of a patient having the target disorder after a diagnostic test result is known. The clinician can calculate the posttesting probability of a disease using the **Bayes theorem**.

3. **The Bayes theorem.** Reverend Thomas Bayes (1702–1761), an English clergyman, developed a method of predicting probability that an event is true given that another event is true. This is referred to as the "notion of conditional probability."
   In medical terms, the Bayes theorem is the probability (P) of a medical hypothesis (H) conditional upon new information or evidence (E). It is expressed mathematically as:

   $$P(H/E) = P(E/H) \times P(H)/P(E)$$

   Another way of expressing this is as follows:

   $$P\ (H/E) = \frac{\text{Probability of the evidence given the hypothesis} \times \text{the probability of the hypothesis}}{\text{The probability of the evidence}}$$

   Therefore, using this theorem the clinician can calculate or estimate the probability of disease based upon the following: (a) pretesting probability of disease, (b) probability of a history of present illness finding and physical examination or laboratory test result conditional upon the patient ***having*** the disease (e.g., sensitivity), and (c) probability of a history of present illness finding and physical examination or laboratory test result conditional upon the patient ***not having*** the disease (e.g., specificity).

B. Incidence and Prevalence

Clinically relevant measures of the frequency of events are usually expressed as fractions in which the ***numerator*** is the number of patients experiencing the outcome (e.g., cases) and the ***denominator*** is the number of people in whom